24 HOURS' AMBULATORY ELECTRO CARDIOGRAPHIC MONITORING IN PATIENTS OF CORONARY ARTERY DISEASE WITH SPECIAL EMPHASIS ON HEART RATE VARIABILITY

THESIS

for

DOCTOR OF MEDICINE

(MEDICINE)

BUNDELKHAND UNIVERSITY

JHANSI (U. P.)

2000 RAJPAL SINGH

CERTIFICATE

This is to certify that the work entitled "***24 HOURS' AMBULATORY ELECTROCARDIOGRAPHIC MONITORING IN PATIENTS OF CORONARY ARTERY DISEASE WITH SPECIAL EMPHASIS ON HEART RATE VARIABILITY***" which is being submitted as a thesis for M.D. (Medicine) Examination 2000, of Bundelkhand University, Jhansi has been carried out by **Dr. Raj Pal Singh** in the Department of Medicine, M.L.B. Medical College, Jhansi

He has put in the necessary stay in the Department as per University regulations.

Dr. R.C. Arora,
M.D., D.Sc.,
Professor & Head,
Department of Medicine,
M.L.B. Medical College,
Jhansi (U.P.),

Dated :

CERTIFICATE

This is to certify that the work entitled "***24 HOURS' AMBULATORY ELECTROCARDIOGRAPHIC MONITORING IN PATIENTS OF CORONARY ARTERY DISEASE WITH SPECIAL EMPHASIS ON HEART RATE VARIABILITY***" which is being submitted as a thesis for M.D. (Medicine) Examination 2000, of Bundelkhand University, Jhansi has been carried out by **Dr. Raj Pal Singh** under my direct guidance and supervision. The techniques embodied in this thesis were under taken by the candidate himself and the observations recorded were checked and verified by me from time to time.

Praveen Jain

Dr. Praveen Kumar Jain
M.D., Dip. Card., DM (Card.)
Professor in Cardiology
Department of Medicine,
M.L.B. Medical College,
Jhansi (U.P.),

Dated :

(Guide)

ACKNOWLEDGEMENT

Acknowledgement of the favour received and privileges enjoyed is not simply a matter of going through a time honoured ritual. It is having the pleasure and satisfaction of discharging various debt of gratitude.

It was my proud privilege to have been associated with and remain under the constant vigilance of Dr. Praveen Kumar Jain, M.D., Dip., Card, DM (Card.) Professor in cardiology, Department of Medicine, M.L.B. Medical College, Jhansi, who provided me an opportunity to perform this work under his guidance. Immensely rich in his field of study and towering presence in intellectual nature, he guided me at every point, with his invaluable suggestions, concrete guidance, constructive criticism and meticulous attention and perfused my brain with his unlimited knowledge. He had always been a source of encouragement, constant inspiration and the ultimate solution for my quaries. For his nobel kindness, selfless generosity and eveready helping nature, I shall remain ever grateful to him.

I would like to express my profound respect and immense gratitude to esteemed and learned Prof. R.C. Arora, MD. Dsc. (Principal Dean, and Head, Department of Medicine, M.L.B. Medical College, Jhansi. His fatherly attitude, valuable suggestions, constructive criticism and meticulous attention have gone a long way towards to success of this work.

It is an immense pleasure to present my deep regards towards Dr. P.K. Jain M.D., MNAMS Professor and Dr. Navneet Agarwal MD, Professor, Dr. N.S. Senger MD, DM (Nephrology) and Dr. Gyanendra Kumar, MD, (Psychiatry) Assistant Professor, Department of Medicine M.L.B. Medical College, Jhansi, for their most precious help, keen interest, invaluable suggestions and constant encouragement in moulding this work to a successful completion.

I express my heartiest thanks for the co-operation extended at every juncture of my work by my friends and colleagues, all the residents of Department of Medicine.

Each cell of my body is indebted to my parents for their constant inspiration and blessing and to my brother and sister for their constant encouragement.

Finally, I wish to thank my wife Dr. (Mrs.) Gouri Singh for Standing beside me at every moment and boosting my moral.

Finally thank all the patients who became the case material for this study and cooperation throughout the follow-up. I am also thank full to Mr. Sunder Lal Kushwaha C/o J.P. Computers for bringing out such a neatly impressive computerised script.

In the last but not the least I pay my sincere prayer to the Almighty God.

Date :

RAJ PAL SINGH

CONTENTS

Introduction

24 HOURS' AMBULATORY ELECTROCARDIOGRAPHIC MONITORING IN PATIENTS OF CORONARY ARTERY DISEASE WITH SPECIAL EMPHASIS ON HEART RATE VARIABILITY

INTRODUCTION

Coronary artery disease is the most common serious chronic life threatening illness in USA where more than 11 million persons have coronary artery disease. It continues to remain the leading cause of mortality and morbidity. Although the prevalence of CAD varies widely throughout the globe, prevalence is lowest in Japan, France and highest in USA & Finland.

Coronary artery disease (CAD) has become a major public health problem in India. CAD is emerging as a major killer in India. Some recent data have suggested that CAD will replace infections as the major killer by the year 2015[1].

CAD has become one of the most common cardiac disorders that affects the adult Indian population. In many cases, CAD afflicts Indians in the prime of their lives. It is well known that the prevalence of CAD increases with age and recent studies have demonstrated that CAD is the leading cause of death in people above 55 years of age[1]. It should, however, be noted that, based on recent observations, the prevalence of CAD in younger age groups (often referred to as premature CAD) appears to be increasing in people of Indian origin. It has been reported that some may develop clinical manifestation of CAD in the second or third decade of life. Even in women who are relatively protected from CAD in the premenopausal period, after 65 years of age CAD becomes the leading cause of death. With improved survival and increased life expectancy the number of patients with CAD is likely to increase[2]. A recent meta. analysis also showed that there has been a Nine fold increase in CHD in urban populations from the 1960s to the 1990s and the two fold increase in rural populations from the 1970s to the 1990s[2]. The meta-analysis also showed

that this increase is more in younger age groups (20-39 years) and it is also affecting men more than women.

Despite the recent increase in the incidence of premature CAD in Indians, little is known about the pathogenesis of atherosclerosis and premature CAD in Indians. Evaluation of major coronary risk factors in Indian patients undergoing coronary arteriography has shown that more than one third of patients with CAD have no major risk factors (Kaul U, Dogra B. Manchanda SC, Am Heart J. 1986[4]. 71:112-115). There is an urgent need to examine the role of environmental factors, metabolic abnormalities, and genetic factors responsible for premature CAD in Indians.

Recent epidemiologic observations have clearly demonstrated that of all ethnic groups, the people of Indian origin have one of the highest incidence of CAD ([5-10]). Most of these studies have also documented that CAD in Indians frequently occur at an early age (usually in prime years the 3rd or 4th decade of life) and the disease is diffuse and severe [11-12]. In addition the results of some studies have shown that when compared with age and gender matched individuals living in a similar geographic location, the Indians with CAD have a significantly increased risk of myocardial infarction and cardiac death (often at a young age), which occur's earlier in the course of the disease process [8-15] the rate of premature CAD has been documented to be upto 3 times higher when compared with people of similar age in western world [16-18]. Of those Indian patients with CAD who are fortunate enough to come to clinical attention before a coronary event occurs, many are considered poor candidates for myocardial revascularization (coronary bypass surgery and coronary angioplasty) because of the diffuse and advanced extent of angiographically demonstrated CAD [15-19].

It is also becoming increasingly apperent that the natural protection for premenopausal women is often lost for many women of Indian origin,

particularly those residing in South Africa and England [19-21]. The predilection for premature CAD in Indian women might well be related to increased incidence of diabetes and obesity and could provide important insight into the basic pathophysiologic process responsible for the accelerated premature CAD in Indians[19-21]. The available data clearly indicate that premature and accelerated CAD is a growing health problem for people of Indian origin 1-9. Although no specific data are available, it seems reasonable to consider that because the disease afflicts most Indian in the prime of their professional careers and early years of family life, it would have significant socioeconomic consequences. Clearly than there is an urgent need to pay close attention to the problem of premature CAD in Indians and define the underlying pathophysiologic processes involved so that potential solutions to resolve the problum can be implemented.

Coronary artery disease has been defined as "Impairment of heart functions due to inadequate blood flow to the heart compared to its needs, caused by atherosclerotic narrowing and occlusion of coronary arteries of the heart" [22] CAD may manifest itself in many ways.

A. Angina pectoris
   - Stable
   - Unstable
     - Prinzmetal's variant
     - Silent ischemia

B. Myocardial infarction
   - Q wave
   - Non Q wave

C. Unexplained arrhythmias
D. Unexplained CCF
E. Abnormal X-ray Chest, ECG, TMT, CART
F. Sudden death

There are only few studies on its prevalence in the general population in India, on screening of persons over the age of 30 years by a 12 lead ECG, in Chandigarth (urban population) the prevalence was found to be 65.4 and 47.8 per 1000 males and females respectively[23]. In rural village in Haryana population the prevalence was 22.8 and 17.3 per 1000 males and females respectively[24]. The current ICMR survey has shown a prevalence rate of about 80-120/1000 and it is estimated that there are about 40 million patients of CAD in our country.

ANGINA PECTORIS :

Angina pectoris is the term used to describe discomfort due to transient myocardial ischemia and constitutes a clinical syndrome rather than a disease, it may occur whenever there is an imbalance between myocardial oxygen supply and myocardial oxygen demand (MVO2). Coronary atheroma is by far the most common cause but angina is also a feature of aortic valve disease, hypertrophic cardiomyopathy and some other forms of heart disease.

STABLE ANGINA :

Presents classically by left sided or central chest pain that is precipitated by exertion and promptly relieved by rest. Most patients describe a sense of oppression or tightness in the chest - "like a band around the chest", pain may be denied . Angina Victim often closes a hand around the throat, puts a hand or clinched fist on the starnum or places both hands across the lower chest. many patients report a choking sensation. Breathlessness in sometimes a prominent feature, the pain may radiate to the neck or Jaw and is often accompanied by discomfort in the arm's particularly the left, the wrists and same time the hands; the patient may also describe a feeling of heaviness or uselessness in the arm. Occasionally the pain is in epigestric or inter scapular . Angina may occur at

any of these places of reference with out chest discomfort but a history of precipitation by effort, and relief by rest or sublingual nitrate should still allow the condition to be recognised.

Symptoms tend to be worse after meal, in the cold, and when walking uphill or against a strong wind. Some patients find that the pain comes when they start walking and later it does not return despite greater effort (start-up angina) (walkthrough angina) some experience the pain when lying flat (decubitus angina), and some are awakened by it (nocturnal angina).

Angina may also occur capriciously as a result of coronary arterial spasm, occasionally this is accompanied by transient ST elevation on the ECG prinzmetal's or variant angina) .

Differential diagnosis of this includes musculoskeletal paricardial and oesophageal pain. musculoskeletal pain are provoked by specific movement rather than by walking and background pain often persist at rest, there may be associated chest wall tenderness. The pain of pericarditis is occasionally provoked by exercise.

Angina occuring at rest may be confused with oesphagitis with or without a hiatus hernia, but pain due to oesophagitis usually has a burning quality and is relieved by antacids, oesophageal spasm, however distinguish from variant angina.

Electrocadiogram may show evidence of previous myocardial infarction but is normal in most patients. Occasionally there is T wave flattening or inversion in some leads providing non-specific evidence of myocardial ischaemia or damage.

UNSTABLE ANGINA :

The term is used to describe patients who present with rapidly worsening angina (cresendo angina), severe angina at rest or prolonged and severe

ischemic chest pain without ECG or enzyme evidence of significant myocardial infarction, it may present as a new phenomenon or against a background of chronic stable angina.

The culprit lesion is usually a complex ulcerated or Fissured atheromatus plaque with adherent Thrombus and local coronary artery spasm. Episodes of myocardial ischemia are due to an abrupt reduction in coronary blood flow caused by thrombosis or spasm .

Supply-led Ischemia) : In contrast the stable angina is related to a fixed obstruction and is usually precipitated by an increase in myocardial oxygen demand. **Demand-led Ischemia) :** ECG usually shows acute ST segment elevation or depression during episodes of myocardial ischemia, the ECG changes are sometimes prolonged.

MYOCARDIAL INFARCTION :

Myocardial infarction generally results from abrupt decrease in coronary blood flow. This generally follows a thrombotic occlusion of a coronary artery previously narrowed by atherosclerosis[25-26]. Infarction occurs when an atherosclerotic plaque fissures, ruptures or ulcerates and with conditions favouring thrombogenesis (factors which may be local or systemic) a mural thrombus forms, leading to coronary artery occlusion. Coronary artery spasm may cause acute myocardial infarction in rare patients with normal coronary arteries. It has been postulated that spasm may cause in final damage that can initiate formation of an atherosclerotic plaque[27]. An association between coronary artery spasm and coronary artery thrombosis has also been documented clinically[28].

I additional infarction may be due to coronary artery occlusion secondary to coronary emboli. The causes of coronary embolism are numerous infective and marantic endocardits, mural thrombi, prosthetic valve fragmentation[29],

neoplasms[30] air that is introduced at the time of cardiac surgery[31] and calcium deposits from manipulation of calcified valves at operation. In thrombosis of coronary arteries can occur secondary to chest wall trauma. Oral contraceptive use to also probably can be associated with acute myocardial infarction in healthy women, the mechanism of this association may operate through an increased tendency of thrombosis Viral infections, particularly with Coxsakie-B may an uncommon cause of AMI[32]. Syphilitic aortitis may produce marked narrowing or occlusion of one or both coronary ostia[33]. Whereas Takayasu arteritis may result in obstruction of coronary arteries[34]. Necrotising arteritis, polyarteritis nodosa[35], muco-cutaneous lymph node syndrome (Kawasaki disease)[36], systemic lupus erythematosus and giantcell arteritis can cause coronary occlusion[37]. Therapeutic levels of mediastinal radiation can cause thickening and hyalinization of the wall of coronary arteries, with subsequent infarction[38], AMI may also be the result of coronary arterial involvement in amyloidosis, Hurler syndrome, pseudoxanthoma elasticum[39] and homocystinurea cocain abuse may cause myocardial infarction in patients with normal coronary arteries, pre-exiting myocardial infarction documented coronary artery disease of known coronary artery spasm [40-41].

A variety of hematological disorders causing in situ thrombosis in the presence of normal coronary arteries such as polycythemia vera, cyanotic heart disease with polycythemia[42], Sickle cell anemia[43], disseminated intravascular cougulation, trhombocytosis and thrombotic thrombocytopenic purpurse, can cause myocardial infarction. The conditions which augment the oxygen demand (Thyrotoxicosis)[44], amphetamine use[45], are also suggested causes, Hypotension secondary to sepsis, blood loss, or pharmacological agents can precipitate myocardial infarction.

Acute myocardial infarction may be precipitated by factors such as severe physical exercise, mental stress and medical or surgical illnesses. Other factors

reported as predisposing to AMI include respiratory tract infection, hypoxaemia of any cause, pulmonary embolism, hypoglycemia, administration of ergot preparations, serum sickness, allergy and wast stings.

A circadian periodicity has been associated to the time of onset of AMI. The early morning hours 6.00 a.m. to 12.00 noon are associated with peak incidence of AMI [46] and parallels the onset of other related phenomena inclding sudden cardiac death. Thrombotic stroke and transient myocardial ischemia. Early morning hours are associated with rise in plasma catecholamines and cortisol and increases in platelet aggregation. The characteristic circadian pattern is absent in patients receiving betablocker or aspirin therapy before their presentation with AMI[47-48].

Acute myocardial infarction may be divided into two types : transmural infarcts in which myocardial necrosis involves the full thickness (or nearly full thickness) of the ventricular wall, and subendocardial (non transmural infarcts, in which myocardial necrosis involves the subendocardium, the intramural myocardium, or both without extending all the way through the ventricular wall to the epicardium[49]. In transmural infarction, occlusive coronary thrombosis is commoner, and localized to the distribution of a single coronary artery. Nontransmural infarctions, frequently occur in the presence of severely narrowed but still patent coronary arteries, severe obstruction occurring before infarction protects against the development of transmural infarction due to development of collateral circulation.

Acute myocardial infarction presents classically as retrosternal or precordial pain, spreading frequently to both sides of the anterior chest, more on left side. The pain radiates down the ulnar aspect of the left arm, producing a tingling sensation in the left wrist, hand, and fingers. The pain is prolonged, usually lasting for more than 30 minutes and frequently for a number of hours. The discomfort is described as constricting crushing, oppressing, or

compressing. The patient complain of a sensation of heavy weight or squeezing in the chest. The pain may also be characterized as a stabbing knife like, boring, or burning discomfort.

The discomfort may radiate to the shoulders, upper extremities, neck, jaw, and interscapular region, again usually favouring the left side. Associated symptoms are dyspnoea, diaphoresis nausea, vomiting belching, diarrhoea and an urge to defecate.

Population studies suggest that between 20 to 60 percent of non-fatal MIs are unrecognized by the patient and are discovered only on subsequent routine electrocadiographic[50-51] or postmortem examinations. Of these unrecognized infarctions, approximately half are truely silent, with the patient unable to recall any symptoms. unrecognized or silent infarction occurs more commonly in patients without antecedent angina pectoris and in patients with diabetes and hypertension. Silent MI is often followed by silent Ischaemia. In elderly patients AMI may present as sudden onset of breathlessness which may progress to pulmonary oedema. Other less common presentations are sudden loss of consciousness and confusional state.

Patients suffering an AMI often appear anxious and in considerable distress. An anguish facial expression is common. Pollor associated with perspiration and coolness of the extremities occurs commonly. Although many patients have a normal pulse rate and blood pressure, within the first hour of infarction, about one Fourth of patients with anterior infarction have manifestations of sympathetic nervous system hyperactivity (tachycardia and/or hypertension), and upto one half with inferior infarction show evidence of parasympathetic hyperactivily (bradycardia and /or hypotension).

The precordium is usually quiet and the apical impulse may be difficult to palpate. In patients with anterior wall infarction, an abnormal systolic pulsation caused by dyskinetic bulging of infarcted myocardium may develop in the

periapical area. Third heart sound (S_3) and fourth heart sound (S_4) may be present along with diminished intensity of S_1 and S_2 Rarely paradaxical splitting of second heart sound can be heard. A transient apical systolic murmur due to mitral regurgitation caused by dysfunction of papillary muscle is commonly audible during acute myocardial infarction. Jugular venous distension occurs commonly in patients with right ventricular infarction, Basilar rales are frequently detected. Temperature upto 38^{0}C may be found towards the end of first week of AMI. Pericardial friction rub is audible along the left sternal border or just inside the point of maximal impulse especially in patients with transmural infarction in approximately 10% cases.

The eletrocardiaographic changes in acute myocardial infarction present as Q waves or loss of R waves in patients with transmural (Q wave MI) and only ST segment and/or T-wave changes in non transmural infarction (non-Q wave MI). total occlusion of the infarct related artery produces ST-segment elevation, and ultimately evolves in a Q-wave MI. A small proportion may sustain only a non Q-wave MI. A minority of patients who present initially without ST-segment elevation may develop a Q- wave infarction.

The initial chest roentgenogram can detect signs of left ventricular failure and cardiomegaly signs of pulmonary congestion may be present.

2D - Echocardiography is a sensitive technique for examining regional left ventricular wall motion. Also useful in diagnosis of right ventricular infarction, ventricular infarction, ventricular aneurysm, pericardial effusion and left ventricular thromboses.

The early use of echocardiography can aid in the early detection of potentially viable but stunned myocardium (contractile reserve)[52], residual provocable ischemia, patients at risk for the development of congestive heart failure following AMI [53], and mechanical complication of AMI.

Doppler echocardiography is useful in detection and quantification a ventricular septal defect and mitral regurgitation, several redionuclide imaging techniques redionuclide angiography, perfusion scintigraphy, infarct avid scintigraphy, ventriculography and positron emission tomography are useful in detecting acute myocardial infarction in assessing the effects of infarct on ventricular function and in establishing prognosis.

The serum cardiac markers are useful indicator for diagnosing acute myocardial infarction. These are released in large quantities into the blood from necrotic heart muscle following myocardial infarction. Among them the important are creatine Kinase (C.K,.), serum aspartate transaminase AST or SGOT lactic dehydrogenase (LDH), cardiac specific troponins and myoglobin.

Creatinine Kinase (CK) rises within 4 to 8 hours following the onset of AMI and declines to normal within 2 to 3 days. The peak CK occurs on average at about 24 hours, CK is not specific because it may also increase in patients with muscle disease, alcohol intoxication, diabetes mellitus, skeletal muscle trauma, vigorous exercise, convulsion intra muscular injections, thoracic outlet syndrome and pulmonary embolism. The isoforms CK-MB_1, and CK MB_2 has been indentified.

In one study an absolute level of the CK- MB_2 Isoform
> 1.0 U/L or ratio of $\underline{CK - MB_2}$ /CK-MB1 > 1.5 had a sensitivity for diagnosis AMI and 59 percent at 2 to 4 hours and of 92 percent at 4 to 6 hours [54].

Serum aspartate transsaminase (AST) starts to rise about 12 hours after infarction and reaches a peak on the first or second day, returning to normal within 3 to 4 days. False positive elevations occur frequently with most hepatic or skeletal muscle diseases, following intramuscular injections, pulmonary embolism & with shock. Because the time course of elevation offers no advantage relative to other serum markers, its incremental benefit for the diagnosis of AMI is negligible, and it is no longer routinely used.

Lactic dehydrogenase (LDH) starts to rise after 24 to 28 hours of the onset of AMI, reaches a peak 3 to 6 days and returns to normal levels 8 to 14 days after the infarction. Total LDH, although sensitive, is not specific, false positive elevations, occur in patients with hemolysis megaloblastic anemia, leukemia, liver disease, hepatic congestion, renal disease, a variety of neoplasms, pulmonary embolism, myocarditis, skeletal muscle disease and shock. LDH comprises of five isoenzymes. LDH_1, is found predominantly in the heart. Therefore increased LDH_1 is a more sensitive indicator of myocardial infarction than total LDH. it's sensitivity exceeds 95 percent. However, LDH isoenzymes need to be measured only when the initial CK or CK - MB elevation might have been missed (after 48 hours). Because they are not more sensitive than CK-MB, newer & more cardiac - specific late markers such as cTnI or cTnT have also emersed.

Myoglobin is a protein released into the circulation from injured myocardial cells and can be demonstrated within few hours after the onset of infarction. Peak levels are reached considerably earlier (1 to 4 hours) than peak values of serum CK [55]. A more rapid rise in serum myoglobin has been observed following reperfusion and its measurement has been suggested as a useful index of successful reperfusion.

Cardiac -Specific Troponins (cTnT and cTnI) are antibodies produced against the cardiac muscle, In patient with AMI, cTnT and cTnI first begin to rise above the upper reference limit by 3 hours from the onset of chest pain. Elevation of cTnI may persists for 7 to 10 days followings AMI elevations of cTnT may persist for upto 10 to 14 days, the kinetics of release of cTnT are similar for patients with Q-wave and non Q-wave AMI [57], patients with AMI who undergo successful recanalization of the infarct - related artery have a rapid release of cTnT, this may be useful as indicator or reperfusion[56,58].

Other promising serum cardiac markers that are under study include heart fatty acid binding protein (hFABP), myocin light chain (MLC), myocin heavy chains (MLC) and glycogen phosphorylase isoenzyme BB (GPBB) [59].

The mortality with acute myocardial infarction is approximately 30 percent with more than half the death occuring before the striken individuals reach the hospital. An additional 5-10% of the survivors of acute myocardial infarction die in the first year, despite major theraputic advances in the treatment of ischaemic heart disease.

In USA, steady decline in the mortality rate from AMI has been observed across several population group[60,61]. This drop in mortality appears to be caused by a fall in the incidence of AMI and a fall in the case fatality rate. Now clinicians are more astute at identifying those patients who are at increased risk of AMI[62] and benefit from more aggrassive prophylactic cardiovascular treatment to prevent it from occuring e.g. use of intravenous nitroglycerine during non cardiac surgery [63].

Several landmarks in the management of patients have contributed to the decline in mortality from AMI [65]. In the mid 1960's the concept of coronary care units was introduced. The first decade of coronary care was notable by detailed analysis and vigorous management of cardiac arrhythmias. Subsequently introduction of the pulmonary artery balloon flotation catheter set the stage for bedside hemodynamic monitoring and more precise management of heart failure and cardiogenic shock associated with AMI. The modern reperfusion era of coronary care was ushered in by intra coronary and than intravenous thrombolysis, increased use of aspirin and the development of primary percutaneous transluminal coronary angioplasty PTCA for AMI [64].

Drugs therapy continues to be an integral aspect of the treatment of patients with AMI, with note worthy advances in the use of beta - adrenoceptor

blockers, antithrombotic regimens, nitrates, and angiotensin converting enzyme (ACE inhibitors) [66].

HOLTER MONITORING : The idea of holter monitoring is three fold[68].

1. Quantitation of ventricular arrhythmias.
2. Heart rate variability (HRV).
3. Silent myocardial Ischaemia (SMI).

Ventricular arrhythmia:

Detection and quantitation :

Holter monitoring is an excellent modality to detect and quantitate ventricular arrhythmia but it has serious limitations in predicting the propensity for recurrence of sudden cardiac death in a given individual. This is better judged by signal average ECG or electro-physiological studies (EPS) the results of ventricular arrhythemia analysis must always be interpreted in light of left ventricular (LV) dysfunction it is the associated (LV) dysfunction (EF<40%) which is more important predictor of SCD than the frequency or complexity of ventricular arrhythmia. In the absence of LV dysfunction, the VPB's howsoever complex they may be, are unlikely to culminate into ventricular tachycardia / ventricular fibrillation.

Detection of SMI :

If there is evidence of myocardial ischemia, this should be treated first before initiating any antiarrhythmic therapy. It is seen that control of myocardial ischemia may result in disappearance of VPB's .

Heart rate variability :

The beat of the healthy heart is not absolutely regular, cyclic variation of the heart rate and arterial blood pressure with respiration was documented as early as the 18th century by Stephen Hales the British botanist .

1. TIME DOMAIN ANALYSIS :

It is based on simple principals, However they are affected by artifacts such as the omission of QRS complexes and do not distinguish clearly between sympathatic and parasympathatic components. Time domain measurement are of two types.

(i) Based on inter beat intervals :

These indices are influenced by both short term factors such as respiration and prolonged factors such as circadian rhythm this category includes :

(a) SDNN - The standard deviation (SD) of all normal RR (NN) intervals, it is also known as the cycle length variability.

(b) SDANN - The standard deviation of the mean of the 5 minutes intervals, averaged over 24 hours.

(c) SDNNIDX - the average of the SDs of inter beat intervals for each 5 minute interval, an intermediate between long term and short term variability

(ii) Based upon comparison of the lengths of adjacent cycles :

These indices predominantly reflect the vagaltone and are almost independent of long terms trends this category includes.

(a) PNN50 - (Ewing index) The percentage of consecutive cycle that are more then 50-MSec. apart.

(b) rMSSD - The root mean square successive differences, which is the square root of the averaged sum of the squared difference, which is the square root of the averaged sum of the squared differences in adjacent NN cycle lengths.

2. FREQUENCY DOMAIN (Spectral) Analysis, Spectral Power) :

Though more difficult to analyse requiring a Holter system with and accurate timing track, more over this analysis is unable to cope with the

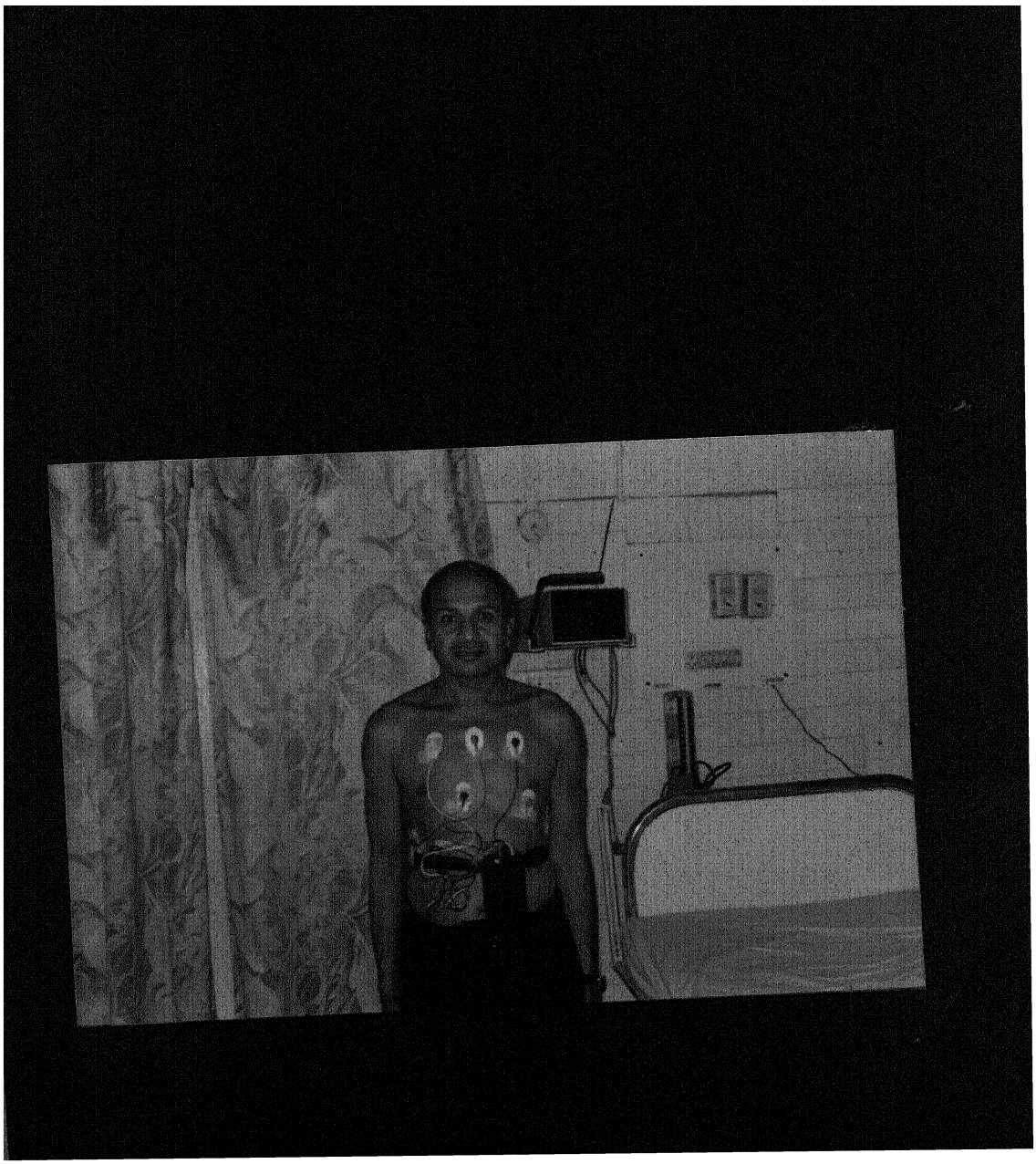
recording containing frequent ventricular arrhythmias. It provides on estimate of the overall variance in heart rate, HRV resulting from periodic oscillation of the heart rate at various frequencies this variance, expressed as $msec^2$ or normalised unit (0-100) is referred to as 'power' in a portion of the total spectrum of frequencies this power spectrum can be classified into different frequency bands as follows.

(i) High frequency (HF) 0.15 to 0.4 Hz : This is parasympathatically mediated and mainly reflects respiratory variation.

(ii) Low frequency (LF) 0.04 to 0.15 Hz : This is modulated by both sympathetic and parasympathetic nervous system and corresponds mainly to vasomotor activity, being strongly affected by baroreceptor activity.

(iii) Very low frequency : 0.003 to 0.04 Hz : This may be affected by the renin angiotension, perepheral vasomotor and thermoregulatory changes.

(iv) Ultra low frequency (ULF) o.00115x10^5 To 0.0033 Hz in addition to the factors affecting UVLF, the ULF is also influenced by circadian rhythm total power (TP) represent the sum of HF, LF, VLF and ULF and is the total variance in the signal. There are is strong correlation between indices of the time domain analysis with those of the frequency domain analysis.



Review of Literature

REVIEW OF LITERATURE

Current indications for the use of Holter monitoring to detect clinically meaningful cardiac arrhythmias.

- Evaluation of patients with syncope, palpitations, or other symptoms that may be due to arrhythmias.
- Evaluation of patients with known arrhythmia in order to improve the quantification of the frequency and or the rate of the rhythmic disorders.
- Evaluation of anti arrhythmic drug efficacy surveillance of the function of implanted pacemakers. During the past decade, there has been a dramatic increase in catheter ablation.

AMBULATORY ISCHEMIA :

Numerous investigators have evaluated the prognostic value of ambulatory ischemia in various categories of CAD patients eg. chronic stable angina, unstable angina and post myocardial infarction.

ST depression during holter monitoring is sensitive marker of ischemia in daily life and is useful quantification of total ischemic burden. Simultaneous ambulatory recording of radionuclide time activity by VEST revealed ST depression in 9 out of 13 patients during episodes of transient fall of ejection fraction[76]. In another study of simultaneous pulmonary arterial (PA) pressure monitoring[77] a significant increase in PA diastolic pressure occured during 1 % episodes of ST depression.

Whether ischemia detection by AECG provides additional prognostic information than that provided by exercise testing is controversial issue. Two successive studies by Mulcany et al[78,79, 14] concluded that exercise testing can identify most patients who are likely to have ischemia during daily life and hence AECG does not make any further contribution to risk stratification. In a

recent study, Paul[80] et al also found that probability of ambulatory ischemia on holter can be predicted by time to onset and maximal ST depression on exercise testing, obviating the need for separate AECG monitoring. AECG one month after episode of unstable angina did not add to the value of exercise test for detection of severe coronary lesions at coronary arteriography[81] Evidence in support of the other side of controversy emerged from a large number of studies. Rocco et al[82] studied 86 patients of chronic stable angina and positive exercise test and found significantly higher cardiac event rate (41% v/s 3%) in those with ambulatory ischemia than those without. Deedwania and Carbajal[83] in a similar study found AECG ischemia as the most powerful predictor of cardiac mortality, similar results emerged from few more studies too. [84-85] Tjivoni et al[86] in a study of post infarction patients found a cardiac event rate of 51% in those with ischemia on both TMT and 8.5% in those with no ischemia Langer et al[87] found no increase in cardiac event rate with exercise induced ischemia but significant increase in adverse cardiac events occured with ST depression on AECG. In a recent observation Goodman et al[88] found that ambulatory ECG ischemia is the best predictor of proximal arterial segment involvement score whereas exercise testing and Myocardial perfusion imaging were predictive of coronary jeopardy score. Therefore weight of evidence as of today indicates that AECG ST- depression provides useful additional prognostic information and is recommended for patient subsets with

(i) Exercise capacity <6 min.

(ii) Onset of ischemia < 6 min.

(iii) Peak HR > 120/min[89]

A large population study[90] demonstrated 16 times relative risk of adverse cardiac events in those with history of CAD and ambulatory ischemia and 4 4 times risk in those with ambulatory ischemia and no history of CAD when compared to subjects without these. In preoperative evaluation study[91] of

patients undergoing non - cardiac surgery, transients ST depression on AECG was the significant predictor of postoperative and long term adverse outcome in multivariate analysis. In another recent population[92] study (n = 6693) a model based on age, history, 12 lead ECG and ST-T and rhythm analysis on AECG predicted sudden coronary death as efficiently as extended models containing information form exercise test, echocardiography, ventriculography and heart rate variability analysis. ASIST, the first randomized trial[96] that evaluated the medical treatment of silent ischemia with atenolol and found that absence of ischemia on AECG at 4 weeks of treatment was the most powerful correlate of event free survival. ACIP study demonstrated a severer from of coronary artery disease (more complex plaques and proximal involvement) in those with ambulatory ischemia[94]. A larger trial of 5000 patients (ACIP - II) is planned to test the hypothesis that treatment of ischemia prevents death and nonfatal infarction.

Data regarding prognostic value of AECG ST - depression in unstable angina patients is also conflicting. Marmur et al[95] found similar cumulative duration of AECG ischemia in patients with and without unfavourable outcome. In a cohort of recent onset agina followed up for 15.8 months, presence of ambulatory ischemia did not predict adverse prognosis[96]. To the contary Gottlieb et al[97,98], in two successive reports found significantly higher incidence of MI or mechanical revascularisation in unstable angina patients with ambulatory ischemia. Another study[99] demonstrated that the higher risk of cardiac events is related to the duration of silent ischemia > 60 min over 24 hrs and was illustrated by a large number of diseased vessels and proximal stenosis in these patients. A recent report[100] of 135 unstable angina patients subjected to early coronary arteriography and 24 hours holter monitoring (4±3 days) demonstrated that ambulatory ischemia > 60 minutes was of incremental value in predicting adverse outcome in addition to the extent of coronary artery

disease and LV function. Overview of all available data suggests that it is the higher duration of ambulatory ischemia rather than its mere presence that predicts prognosis in unstable angina.

In post infarction patients, studies by Goldberg[101] and Arstall et al[102] did not find any justification of routine ambulatory ECG monitoring at discharge because of similar adverse events at follow up in those with and without ambulatory ischemia. To the contrary a study of high risk early post infarction patients[103] (LVEF<40%) and ventricular arrhythmia> Lown class III) demonstrated hat ischemia on holter is the most powerful predictor of 1 year mortality. Tzivoni et al[104] also confirmed adverse prognostic influence of ambulatory ischemia which persisted till 2 years after infarction. In a recent randomized trial of [105] tPA versus placebo in acute myocardial infarction. In addition to ejection fraction. ST depression on holter emerged as an independent predictor of VPC frequency suggesting that the underlying extent of both infarcted and ischemic myocardium is important in modulating ventricular arrhythmia after myocardial infarction. Above study[105] found higher frequency and duration of ambulatory ischemia after thrombolysis in those with patent infarct related artery, complex lesion morphology and three vessel disease Krucoff et al[106] in a study of 46 patients thrombolysed with streptokinase found that achievement of ST steady state within 100 minutes of thrombolysis was 89% sensitive and 82% specific for successful reperfusion whereas ST steady state before thrombolysis was 100% sensitive and specific for subtotal occlusion of infarct related artery identifying ambulatory ischemia as an excellent marker of coronary patency.

Mechanical revascularisation by PTCA or CABG leads to significant reduction of ambulatory ischemia. ST changes in these subgroups do not correlate with adverse out come[107, 108, 109]

Post-infarction Arrhythmia

Ambulatory ECG monitoring discloses ventricular arrhythmia in 50 - 60% of post MI survivors just before hospital discharge, the variation in prevalence being related to differing duration of holter monitoring[110-114]. All these five studies of prethrombolysis era have shown ventricular arrhythmias to be of independent prognostic value in predicting sudden death and total cardiac mortality. None of these studies predicted the mechanism of death. The prevalence of ventricular arrhythmia is markedly reduced by thrombolysis[115]. Optimal duration of monitoring for satisfactory detection of arrhythmia is debatable Kennedy et al[116] performed 48 hours of AECG monitoring and found that maximum Lown grading occured in 80% patients during first 24 hours suggested that 24 hours of monitoring should suffice. Another recent report[117] suggested that no further information is obtained from AECG monitoring extended beyond one hour.

Heart rate variability (HRV)

In recent study[118] respiratory sinus arrhythmia (RSA) calculated from the mean absolute difference between successive heart beats was identified an exclusive measure of cardiac vagal tone any may offer advantages over other indices as a prognostic tool. All measures of RR variability were significantly higher in healthy middle aged persons than those with 2 weeks and 1 year after myocardial infarction to such an extent that RR variability can be used for reliable screening of middle - aged populations to predict increased risk of coronary death[119], comparison of 20 patients with angiographically proven CAD with 20 healthy controls revealed no quantitative difference in HRV indices but the normal circadian variation and increase on awakening were blunted in CAD group suggesting some alteration in cardiac neural regulation even in uncomplicated CAD[120]. In another recent study, no correlation of HRV

was found with the mere presence of CAD but a direct correlation with LVEF and inverse correlation with NYHA class emerged[121]. Significant decrease in HF power and therefore an increase in LF/HF ratio was found during 30 minutes before ishcemia episodes when compared to non ischemia points on AECG[122]. This decrease in vagal tone may reflect decreased threshold for dialy life ischemia. Estimation of heart rate variability provides a prognostic information beyond that provided by traditional risk factors. A 9 year follow up study[123] involving an elderly cohart of 736 original subjects of Framingham Heart study revealed that after adjustment of traditional risk factors. HRV indices of VLF, LF, HF, total power and SDNN indices were significantly associated with all cause mortality. Alterations in cardiac geometry by ischemia or infarction lead to derangement in autonomic control of heart rate and reduction in HRV by influencing afferent sympathetic mechanoreceptor discharge. Patretta et al[124] evaluated 32 patients of single vessel disease before and 16-24 days after PTCA. Pre PTCA HRV indices were reduced only in those with regional wall motion abnormalities and increased significantly after PTCA, Simultaneous with improvement in their regional wall motion score.

In a study of unstable angina patients, reduced time domain indices predicted mortality and total cardiac events, SDANN being the most powerful index[125]. Since decreased HRV correlates with increased sympathetic and decreased parasympathtic activity, it could contribute to increase coronary hyper reactivity and atherosclerotic plaque distruption. Valkama et al[126] compared frequency domain measurements of HRV during early (0-12 hours) and convalescent (after 1 week) phase of acute myocardial infarction. In early phase interior location of infarct was associated with more reduction in HRV compared to anterior location whereas in convalescent phase, low ejection fraction and presence of non sustained ventricular tachycardia correlated with reduced total power, LF and VLF indices. Results of this study indicate a

propensity to arrhythmias in those with reduced HRV. In another study[127] from the same group that comprised of 54 CAD patients with either sustained ventricular tachycardia or history of cardiac arrest, impaired LF and VLF indices of HRV reflected suceptibility to spontaneous but not to inducible ventricular arrhythmias. In a temporal profile study reduced HRV at hospital discharge emerged as independent predictor of total cardiac mortality only during first six months in 433 survivors of first myocardial infarction followed up for five years[128] . Data from Vaishnav et al[129] confirmed the association between low HRV and mortality after acute myocardial infarction and suggested that in reflects an imbalance of sympathovagal function independent of LV function thrombolysis in acute myocardial infarction decreases arrhythmic events and electrical heart stability as elucidated by electrophysiological studies and increased HRV indices[130] .

Zebel et al[131] studied the effect of thrombolysis on temporal pattern of HRV changes and found that pNN 50 a time domain parameter indicative of increased vagal tone is increased during first hour in those with angiographically proven successful thrombolysis but this benefit was no longer seen at 24 hours analysis. Merchant et al[132] compared HRV in chronic stable angina with early post infarction patients and found that silent ischemia in stable angina group is associated with reduced HRV whereas such a difference did not emerge in post -infarction group. Probably it is the autonomic dysfunction that is responsible for silent nature of ischemia in stable angina group whereas in post infarction group some other factors may be responsible.

Treatment with metoprolol or atenolol leads to significant and similar increased in heart rate variability in patients with stable coronary artery disease[133] and 4 weeks after myocardial infarction[134] which may account for beneficial effect of beta blockers in these subgroups of CAD.

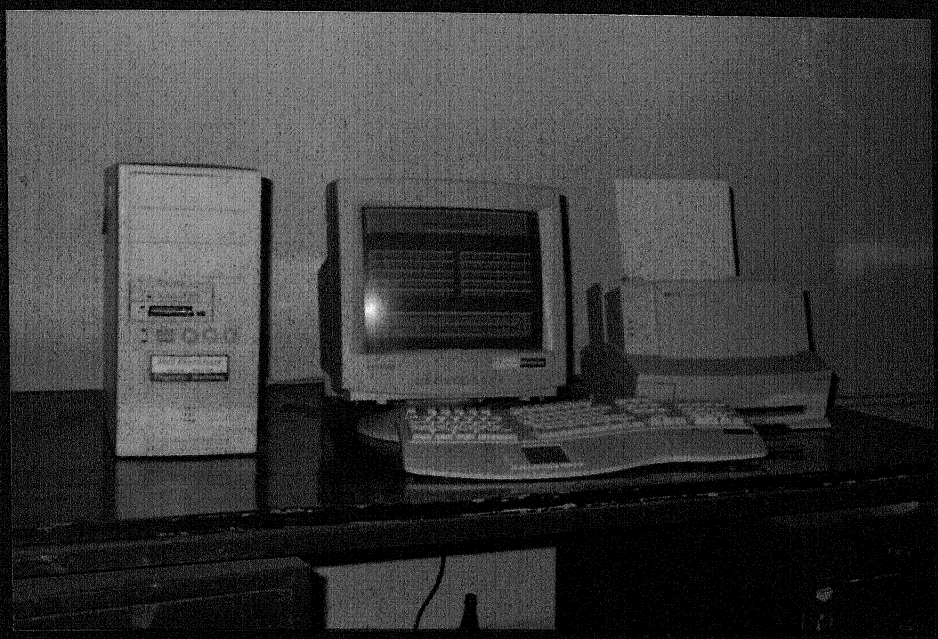
Aims & Objectives

AIMS AND OBJECTIVES

1. To study the arrhythmias in coronary artery disease patients.

2. To evaluate silent and symptomatic myocardial ischemia.

3. To study the heart rate variability in coronary artery disease patients by 24 hours ambulatory Electrocardiography.




DMS

Material & Methods

MATERIAL AND METHODS

The present study was conducted in the Department of Medicine, Maharani Laxmi Bai Medical College, Jhansi over a period of twelve months (March 1999 to Feb. 2000). The patients were taken from Intensive coronary care unit cardiology ward and cardiology OPD.

This study was aimed at 24 hours ambulatory electrocardiographic monitoring of coronary artery disease patients the carieteria of diagnosis of coronary artery disease was.

1. Symptoms suggestive of ischemic heart disease.
2. ECGs Changes suggestive of myocardial ischemia.
   - For confermation any of the following were present –
   - Positive TMT
   - Echocardiographic evidence of ischemia
   - Documented myocardial infarction by ECG0.
   - Myocardial infarction was suspected clinically and confirmed by ECG changes or by an increase in creatinine kinase of > 2 times. Normal total with an associated increase in M.B. isoenzyme to > 5% of total creatinine kinase.
   - Patient of unstable angina were also included in this study, unstable angina was defined as resting prolonged (15 to 30 minutes) new onset angina.
   - Resting angina occuring in patients with either a previous chronic stable angina or with a history of previous myocardial infarction.
   - Worsening effort angina i.e. effort angina that occured in the last few days at a lower threshold and with a higher frequency in patient with previous stable angina furthermore as an inclusion criterion, all

patients enrolled in this study had history suggestive of at least one episode of angina pectoris.

- The Holter monitor analysing done to room is fully Air conditioned maintain requisite temperature and humidity for optimum functioning the Holter Machine.
- This Holter system was built by MEDELEC System Pvt. Ltd. Company from U.S.A.

It had following parts : -

i. HOLTER MONITOR :

Model full Disclosure Holter Analyser System with Digital Solid state Holter Recorders by Diagnostic Monitoring System, USA.

System features : All the system features are the same as model full disclosure cassette Holter analyser system by diagnostic monitoring system USA consisting of -

- Full computerised main Analyser unit with hard Disk Drive (S.No. DMS 8255)
- Enhanced Alpa-numaric key board. (Model EKB 804TP, S.No. 6000883)
- High Resolution 14'' full colour vedio monitor model 4 Bni SAMTRON by SAMSUNG (S. No. HMF 1722876 J).
- High Resolution Hewlett Packard Laser Jet Printer Model C 3990A (HPL J6L) S.No. JPZPI 59368 .

ii. Digital Holter Recorder :

Model DL 700 FC light weight 3 channel solid state digital Holter Recorder with all accessories (Serial No. D 10186).

- Solid State Memory Card
- Patient lead set
- Carrying case W/bell

PRE-REQUISITES FOR TEST :

- Disposable ECG electrodes
- Adhesive tape, shaving rajor and blade
- 2 Dry Alkaline battery pencil size (1.5 volt).

Source of patients :

The subjects for Holter monitoring were selected from the patients who attended cardiology OPD and also from those admitted in ICCU or wards.

Instructions to the Patients :

i. Record your activity every 1/2 hour when you are awake.

ii. If you have any complaints, please write the same with time.

iii. Continue with your daily activities in usual way.

iv. Continue with the medicines as advised by your doctor.

v. The patient was given a chart to note down his half hourly activity and complaints (if any) during the full recording period. In case of any chest pain or discomfort, the patients was asked to click /press the event marker provided with the Holter recorder so that the corresponding ECG, may be very accurately analysed.

vi. He/She was encouraged to be fully relaxed .

vii. Try to be back with in 24 hours as recording cassette will stop after that.

- To begin with the patient was fully explained about the procedure of the test and was asked to wear an loose fitting cotton cloth (especially in summer) over chest.
- Before applying the chest electrodes the chest was properly shaved to remove any hair and the part throughly cleaned with spirit, after this the patient was instructed to wear a loose fitting cloth over chest. Than the various chest electrodes were applied as given below.
- 1. White colour : In the 2nd right intercostal space in mid clavicular line.

2. Blue colour : On manubrium Sterni,

3. Black colour : In the 2nd left intercostal space in mid clavicular line.
4. Brown colour : At the xyphisternum.
5. Orange colour : In the left 4th ICS on mid clavicular line.
6. Red colour : In the left 5th ICS on Anterior Axillary line.
7. Grean colour : In lower most midaxillary line on right side.

The holter monitor was removed exactly after 24 hours after switching the computer system on. The various commands were given by the computer were executed till the screen displayed instruction to insert the flash card. The system takes few seconds to scan the flash card and if the recording has been proper, accepts it. Than the data regarding the patients identification, diagnosis referring physician and medication are typed in, and proper data and time of recording entered in. After completing the above steps the computer takes 2-3 minutes to down - load the data on the disk. This is followed by documentation on the following information on computer screen in the following order, which are edited in the proper way.

1. Time of Holter recording.
2. Heart rate variability data.
3. All potential VE's are displayed along with these timing and number followed by all potential SVE's displayed along with there number and timing.
4. After this significant event ECG strips are shown which includes, ventricular ectopics, ventricular ectopics in pair, supra-ventricular run's aberrent beats etc.
5. This is followed by displaying of the number and timing of all ST elevation or depression.
6. In the last maximum and minimum heart rates are shown on the screen during the24 hours.

After doring this above editing the computer is asked to summerise all the data and printout the report, This analysed data were also reviewed by cardiologist.

A complete medical history was recorded. The history included a definite postal address, phone number, it any, Name of persons who shall provide information about the patient in case of mishap, risk factor's and the history of present illness. History of past illness example hypertension, diabetes mellitus, chronic renal failure or any chronic disease was noted.

A complete examination was done at the time of admission. The patients selected for this study were investigated for the following.

Routine :

a. Complete hemogram.
b. Blood sugar - fasting and post prandial.
c. Blood urea.
d. Serum creatinine.
e. Serum cholesterol, triglyceride (12-24 hours fasting).

Special :

a. Creatinine phosphokinase (CPK-MB).
b. Serum aspartate transaminase (AST).
c. 12 leads standard resting ECG.
d. X-ray chest P.A. view
e. 2 D Echocardiography with Colour Doppler
f. Tread mill test

Were done during follow up when feasible

All patients were followed up every 2 weeks for a month and than every month in cardiology clinic for a period of 6 months or more. In case of patient not attending cardiology clinic contact was made by post or telephonic enquiry.

The Supraventricular arrhythmia in the setting of acute myocardial infarction are classified according to their complexity table 1 [135]

Table I: Classification of supraventricular arrhythmia in AMI

Class 0 = No arrhythmia, 5 or less Premature beats/hr

Class 1 = between 5-100 premature beats/hr.

Class II = > 100 premature beats/hr. or repetitive premature beats.

Class III = atrial or junctional tachycardia

Class IV = Atrial flutter or fibrillation.

Class II,III,IV are defined as complex supra-ventriacular arrhythmia, class III & IV patients have a poorer prognosis as compared to the class I and class II patients.

Table II Lown's classification of ventricular premature beats -

Grade	VPBs
0	None
I	< 30 per hour
II	> 30 per hour
III	Multiform
IV a	Couplets
IV b	3 or more consecutive
V	R-on-T Phenomenon.

Closely coupled VPCs and R-on-T phenomenon were considered the most serious forms predisposing to malignant ventricular arrhythmias. However, it has been observed that late coupled VPBs are also responsible for 41-45% of Clinical episodes of ventricular fibrillation (VF) and in 40-83% cases the VF occurs without any preceding VPBs.

Observations

OBSERVATION

The present study was carried out in the Cardiology Division of Department of Medicine, M.L.B. Medical College, Jhansi. The case material consisted of 45 consecutive patients, with coronary artery disease (Angina/MI), admitted to the intensive coronary care unit (ICCU), ward and cardiology OPD.

GENERAL CHARACTERSTICS OF THE PATIENTS

Table-I Distribution of patients according to their age and sex.

Age groups (years)	Male	Female	TOTAL	
			No.	Percentage
< 35	0	1	1	02.22
35 - 45	6	6	12	26.66
46-55	6	2	8	17.77
56-65	10	3	13	28.88
66-75	8	2	10	22.22
> 75	1	0	1	02.22
TOTAL	**31**	**14**	**45**	**100**

Table -I shows that group consisted of 45 patients 31(68.88%) males and 14(31.11%) Females. Maximum 13 (28.88%) number of patients were from 56 to 65 years of age, including 10 (22.22%) males and 3 (6.66%) females. Mean age of patients in this group was 55.64±12.35 S.D. years.

Table-II Distribution of patients according to site of infarction and Angina pectoris.

Site of Infaction and angina Pactoris	No.	Percentage %
Myocardial Infarction	19	42.22
Anterior	12	26.66
Inferior	3	06.66
Multiple location (Ant+Inferior)	4	08.88
Angina Pectoris	26	57.77
Slabe	10	22.22
Unstable	16	35.55

Table-II shows this group consisted of 45 patients maximum 26 (57.77%) patients had Angina Pectoris including 16 (35.55%) unstable angina and 10 (22.22%) stable angina. 19 (42.22%) were M.I. out of these 12 (26.66%) patients had Anterior wall infarction 3 (6.66%) had Inferior wall infarction 4 (8.88%) patients had infarction at multiple locations.

Table-III Distribution of Subjects in relation with coronary risk factors.

Risk Factors	No. of cases	Percentage %
Cigarette smoking	27	60 %
Hypertension	10	22.22%
Diabetes Mellitus	8	17.77%
Obesity	4	8.88 %
Family history of premature CAD	6	13.33 %
Tobacco Chewing	16	35.55 %

Table-III shows the risk factor wise distribution of patient in this group Cigarette Smoking (60%) was the most common risk factor followed by tobacco chewing (35.55%) Hypertension was present in (22.22%) and diabetes mellitus was present in (17.77%). The family history of premature CAD was present (13.33%. obesity was present in (8.88%). Four patients were without any coronary risk factors.

Table -IV Correlation of Heart Rate Variability (Standard Deviation of R-R Interval) After MI and Angina Pactoris.

Standard Deviation of R-R of normal Cycles (Ms)	No. of Patient	Percent - age	M.I. (19)		Angina Pectoris (26)	
			No.	%	No.	%
0-50	0	0	0	0	0	0
50-100	27	60 %	13	68.42	14	53.84
> 100	18	40 %	6	31.57	12	46.15
TOTAL	**45**	**100 %**	**19**	**42.22**	**26**	**57.77**

Table -IV shows the distribution of Heart Rate Variability less than 50 ms had no subject, 50-100 ms was 60% and more than 100 ms was 40% . Distribtion of subjects according to their disease out of 45 cases 19 (42.22%) belongs to M.I. and 26 (57.77%) of Angina Pectoris. Out of these in 50-100 ms SDNN category HRV was found to be 13 cases (68.42%), 14 cases (53.84%) in M.I. and Angina respectively, and more than 100 ms SDNN category showed 6 cases (31.57%) 12 cases (46.15%) respectively in MI and Angina. According to data shown in table IV post MI patients were found to have higher risk for mortality in comparison to Angina patients.

Table -V Distribution of Prevelance of Ventricular arrhythmias in following groups.

Ventricular Arrhythmias	M.I. (19)		Angina Pectoris (26)		Total	%
VE Pairs	8	42.10%	7	26.92%	15	33.33%
VE Run	4	21.05%	6	23.07%	10	22.22%
VPCs						
>10	8	42.10%	10	38.46%	18	40 %
< 10	11	57.89%	16	61. 53 %	27	60 %
VT	7	36.84 %	4	15.38 %	11	24.44 %

Table -V shows According to above table out of 19 patients of MI 8 had VE pair, 4 had VE run and 8 patient had VPCs less than 10/hrs, 11 had more than 10 /hr and 7 patients had VT.

Out of 26 patients of Angina 7 patients were found VE pair and 6 VE run 10 patients had VPCs less than 10/hrs, and 4 had VT, above data showed that ventricular arrhythmia prevalence more in MI than angina patients.

Table -VI Distribution of Ventricular Arrhythmia According to Lown's classification of VPBs in different group

VPBs	MI (19)		Angina Pectoris (26)	
< 30 Grade -I	4	21.05 %	6	23.07%
> 30 Grade -II	4	21.05 %	6	23.07%

Table VI shows that out of 19 patients of MI 4 had no. of VPBs less than 30 (grade I lown's classification) and other 4 had VPBs greater than 30 (grade II lown's classification). That out of 26 patients of angina there were 6 patients each grade-I and grade-II.

Table -VII Distribution of Supra Ventricular Arrhythmia According to the classification of SVPBs in different groups.

SVPBs	MI (19)	Angina Pectoris (26)
0 -5	17	23
5 - 100	0	4
> 100	1	0

Table - VII shows that out of 19 patients of MI only one patient had SVPBs of grade II (i.e. more than 100) and 17 patients had no SVPBs. Out of 26 patients of Angina only four patients had SVPBs of grade - I (i.e. 5-100) and 23 patients had no SVPBs.

Table -VIII Distribution of Incidence of ST depression in following groups

ST. Depression (≥1mm)	MI (19)		Angina Pecstoris (26)		Total	
	Present	Absent	Present	Absent	Present	Absent
	8	11	9	17	8+9=17	11+17=28
	42.10%	57.89%	34.61%	65.38%	37.77%	62.22%

Table -VIII shows the patient in whom ST depression of 1mm or more was observed .

Out of 19 patients of MI only 8 (42.10%) patients has significant ST depression (i.e. ≥1 mm) on the other hand out of 26 patients of angina, 9 patients had significant ST depression (34.66%). According to Table-VIII significant ST depression was found more in patient with MI rather than with those of Angia.

It may be noted that although none of the patient complained of chest discomfort or pain during 24 hrs Holter recording, some of them had significant ST depression which may indicate silent Ischemia.

Discussion

DISCUSSION

Coronary artery disease has been reported to be on the increase in India in recent times. Various studies indicate that incidence of CAD ranges from 6 to 20% of all heart disease patients (Sinha 1978).

The prevalence of coronary artery disease is more common in males as compared to females the ratio being 4:1, but it is not so at extreme of age when the CAD incidence becomes more or less same in both sexes. In India CAD appears a decade earlier in life as compared to developed countries .

Coronary risk factors play a very important role in development and severity of coronary artery disease.

Those patients who have multiple coronary risk factors are very much prone to develop coronary artery disease.

The present study was conducted in the cardiology division of Deptt. of Medicine M.L.B. Medical College, Jhansi from March 1999 to Feb. 2000.

45 patients were selected for this study Number of male patients was 31(68.88%) and 14 were females (31.11%). Maximum (28.88%) number of patients were from 56-65 years of age, including 10(22.22%) males and 3(6.66%) females. Mean age of the patients was 55.64±12.35 years.

Majority of patients belonged to middle class and with most of them were from urban area, only 10(22.22%) patients were from rural area. Most of the male subjects were from service class while most females were housewives.

Some of the patients in this study were sedentary of which majority were females.

In the present study risk factors for CAD were present in good number of cases (91%), and only four patients were without any known coronary risk factors. Cigarette smoking was observed to be the commonest risk factors (60%) followed by tobacco chewing (35.55%) and hypertension (22.22%) respectively.

HEART RATE VARIABILITY :

Analysis of the variability of RR Interval (HRV) has been shown to be a reliable method to assess cardiac autonomic activity[136-139] . Several recent study have demonstated that a low heart rate variability suggests a reduction in vagal activity with an absolute or relative adrenargic predominance as an independent prognostic determinant in patient with acutes myocardial infarction[140-143]. Several previous studies have shown that a decreased global heart rate variability is a powerful independent prognostic determinant in patients with acute myocardial infarction[140-143].

Kleiger et al[140] first reported that a standared deviation of RR interval < 50 ms an 24 hours Holter recording was associated with a four fold increase in the risk of death compared to patients with standard deviation > 100ms. On the other hand standard deviation between 50-100 ms associated with moderate risk. Present study has some resemblance with the Kleiger et al study. In this study it found that most of the subjects with MI & Angina were in the category of 50-100 ms RR interval standard deviation and these people have moderate risk of developing further complication and mortality.

Increased sympathetic or decreased parasympathetic nervous system activity is reflected in increased indices of heart rate variability. Importantly decreased indices of heart rate variability shown great value as predictor of

mortality in various clinical populations[144]. Decreased heart rate variability (CLV<50 ms) was reported to be an independent risk factor for mortality post MI by the multi-center post infarction project (MPIP) in 1987 [145].

Since then, numerous investigators have corroborated this finding[145-146]. In addition, among survivors of acute myocardial infarction (MI). Bigger et al [147]. and Farrell et al[148] have both shown that decreased heart rate variability predicted both death and arrhythmic events with greater sensitivity and specificity than conventional predictors such as left ventricular ejection fraction.

Low heart rate variability has also been reported to predict mortality among patients, undergoing coronary angiography. Rich et al[149] reported that in 100 stable patients who initially had elective angiography none had an MI within 4 weeks. Non ischemic cardiomyopathy, or valvular disease , SDNN < 50 ms was associated with an eighteen fold 1 year mortality compared with patients with an SDNN more than 50 ms. In patients awaiting cardiac transplantation SDANN <55 ms identified patients at a twenty fold increased risk of mortality[150].

Previous work has shown that reduced RR variability after myocardial infarction is predictive of arrhythmic events [145,146,148,151], sudden death [145, 146, 148,151] and all cause cardiac mortality [145-151] the available data is limited, however in that these studies have generally used a single time domain analysis, either the standard deviation of the individual RR interval[145].

Among time domain indices a lower SDNN is a significant and independent predictor of all cause mortality and of progressive heart failure deaths. A reduced heart rate variability has been observed consistently in patient

with cardiac failure. Present data confirm that a simple and easily measured time domain index of autonomic activity SDNN, has independent prognostic value in patients with angina and MI. It identified an increased risk for all cause mortality in these patients.

Recently, three studies have provide the prognostic value of SDNN in MI and angina . Ponikonski et al found depressed SDNN (<100ms) was independent predictor of cardiac death.

TO EVALUATE SILENT AND SYMPTOMATIC MYOCARDIAL ISCHEMIA

Numerous investigators have evaluated the prognostic value of ambulatory ischemia in various categories of CAD patients eg. chronic stable angina, unstable angina, post myocardial infarction

ST depression during holter monitoring is a sensitive marker of ischemia in daily life and is useful in quantification of total ischemic burden (silent +clinical ischemia).

Whether ischemia detection by Holter monitoring provides additional prognostic information than provided by exercise testing is a controversial issue. Two successive studies by Mulcany et al[78-79] (Reported in Am J. cardiology 1989) concluded that excercise testing can identify most patients who are likely to have ischemia during daily life an AECG does not make only further contribution to risk stratification, in the recent study Paul et al[80] (AJ of Cardiology 1994) also found that probability of ambulatory ischemia on holter can be predicted by time to onset and maximal ST depression on exercise testing obviating the need for separate Ambulatory ECG monitoring. Hotler monitoring one month after episode of unstable angina did not add to the value

of excercise test for detection if severe coronary lesion at coronary artereographic[80] evidence in support of the other side of controversy emerged from a large number of studies. Rocco et al (Cer 1988) studied 86 patient of chronic stable angina and positive exercise test and found significantly higher cardiac events rate (41% Vs 3%) in those with ambulatory Ischemia documented during Holter monitoring than those without.

Deedwania and carbajal[83] (Am. J. of Cardio 1991) in a similar study found ambulatory ECG ischemia as the most powerful predictor of cardiac mortality similar results emerged from few more studies too.

Tjivoni et al[86] in a study of post infarction patients, found a cardiac event rate of 51% in those with ischemia on both TMT and Holter and 8.5% in those with no ischmia on Holter. In a recent observation Good Men et al[88] (Am J Car. 1994) found that ambulatory ECG ischemia is the best predictor of proximal arterial segment involvement score whereas exercise testing and myocardial perfusion imaging were predictive of coronary geopardy score. Therefore weight of evidence as of today indicates that Holter ST depression provides useful additional prognostic information with -

1. Exercise Capacity < 6 min
2. Onset of ischemia < 6 min.
3. Peak Heart Rate >120 min[89].

The present study[90] of Holter monitoring in patients of myocardial infarction and angina pectoris we had 19 patients of myocardial infarction and 26 patients of angina pactoris ST depression ≥1 mm was seen in 8 out of 19 patients (i.e. 42%) while ST depression was absent in 57.89% patient of MI. On

comparison only 34.61% of patient of angina pectoris demonstrated significant ST depression (i.e. ST dep ≥ 1mm) during Holter monitoring.

Thus the incidence of ambulatory significant ST depression was more in patients of myocardial infarction than in patients of angina pectoris although the difference was not statistically significant probably it would have required a very large number of patients in both subgroups to show a significant ST depression incidence difference in patient of myocardial ischemia and angina pectoris. This was most probably the reason why the present study could not demonstrate significantly more incidence of ≥1mm ST depression in patients of myocardial infarction compared to patient with angina pectoris .

AECG monitoring for ST shift is more complex than arrhythmia detection because of significant variability with posture, activity and distortion factors like phase shift, narrow band width low signal to noise ratio and poor low frequency response.

The role of routine Holter monitoring in detecting coronary artery disease in a total asymptomatic population remain unclear .

SILENT ISCHEMIA :

The patho physiology of recurrent ischemic events after infarction often involves an unstable atherosclerotic lesion, which when disrupted, becomes the site of platelet aggregation, coronary vasoconstriction and thrombosis similar ischemic episodes, many of which are asymptomatic and occur at rest, can be identified by ischemic ST changes on continuous electrocardiographic (Holter) monitoring. Previous studies that correlated these changes with abnormalities of myocardial perfusion and function indicate that they represent true ischemic

events. Ischemic ST changes on Holter monitoring predict recurrent ishcemic events in patients with unstable angina as well.

The goal of the present study was to examine the prognostic significance of ischemic ST changes recorded on 24 hours electrocardiographic monitoring before hospital discharge in the context of other clinical variables with regard to mortality and re-infarction in post-infarction population.

The 24 hours Holter monitoring recording tapes were scanned by one experienced doctor for the presence, frequency, and duration of ishcemic ST episode, which were defined as transient ST segment depression of 1mm or greater from the baseline .08 sec. after the J point, lasting by at least 1 minute of isoelectric ST segment. Episode of ST segment elevation were not detected in this population of patients.

To study the incidence of ventricular arrhythemia :

Cardiac rhythm abnormalities occurs in 72-96% of patients with acute MI (Carlson MD, Mackall et al 1998). These comprise of supraventicular and ventricular premature beats, bradyarrhythmias and tachyarrhythmias. Ventriculartachy arrhythmias such as sustained ventricular tachycardia, ventricular flutter and fibrillation are potentially the most dangerous arrhythmias associated with AMI and these may occur in upto 10-50% of all patients with AMI.

Holter monitoring has emerged as an indispensible tool for detection and quantification of ventricular arrhythmias and judging the efficacy of treatment.

Ventricular premature beats (VPBs) are ubiquitous and even short runs of ventricular tachycardia (VT) may be seen in asymptomatic people. In normal,

healthy subjects aged 10-30 years, the incidence of VT defined as three or more consecutive VPBs - is in the range of 1-3%.

The prevalence of frequent VPBs increases with age, as does the prevalence of ventricular couplets and VT multivariate analysis has shown that there is higher prevalence of ventricular arrhythmias including combination of VT and at least 15 VPBs per hour in subjects with an abnormal left ventricular ejection fraction. The development and commercial availability of 24 hours ambulatory ECG recording (Holter monitoring) has made it possible to study the relationship between the frequency and complexity of ventricular arrythmias after myocardial infarction and subsequent mortality. According to available data ony 15-25% of patients have 10 or more VPBs per hour. Mortality rates are 2.5-4 times as great for patients with atleast 10 VPBs per hour in a 24 hours ECG recording in comparison with lower VPBs frequencies.

In addition pairs or runs of VPBs are associated with death independent of VPBs frequency. Transient VT defined as at least three consecutive ventricular beats at a rate of > 100 b pm) occuring on a predischarge 24-hrs ECG recording has a strong relationship with subsequent mortality only about 12% of patients.

In the present study 19 patients of MI and 26 patients of angina pectoris 24 hours recording, revealed higher incidence of ventricular arrhythmias in patients with myocardial infarction as compared to angina pectoris.

In the present study 19 patients of MI and 26 patients of angina pectoris 24 hours Holder recording higher incidence of ectopics were seen in 8 patients 42.10% and 10 patients 38.46%. Ventricular couplets in 8 patients 42.10%

and 7 patients 27.92% and ventricular runs in 4 patients 21.05% and 6 patients 23.07% respectively in patient of AMI & angina pectoris in difference however could not reach upto statistical significant because of small number of patients.

In patients of AMI VPCs > 10 per hour, were seen in 42.10% patients and <10VPCs per hour were seen in 57.89% patients. The corresponding values in patients of angina pectoris were 38.46% and 61.53% respectively.

The greatest significant difference of ventricular arrhythmias is seen when the study compare incidence of ventricular taecycardia (VT) in both groups the incidence of ventricular taechycardia during 24 hours ambulatory ECG recording is 36.84 % in patients of myocardial infarction, while it is only 15.38% in patients of angina pectoris. In present study when VPBs were classified according to Lown's classsification the percentage of patients in lown's classification grade I and II was 21.05% each. the corresponding percentage of grade I and grade II VPBs in patients of stable angina pectoris was 23.07% each.

Hence this study conclude that all type of ventricular arrhythmias detected during Holter monitoring are more common in patients of myocardial infarction in comparison to patients of angina pectoris. These increased incidences of ventricular arrhythmias during Holter monitoring in patients of myocardial infarction are also indicates of these increased risk of mortality in comparison to patients of Angina pectoris.

Study the incidence of Supraventricular Arrhythmias according to the classification of SVPBs :

The role of ventricular arrhythmias associated with acute myocardial infarction is well appreciated. However, the genesis and effects of supraventricular techyarrythmias (SVTs) associated with acute myocardial infarction (AMI) is still a subject of controversy 1. (Lown B Klein MD et al Am J Med 1969).

The incidence of Supraventricular arrhythmias varies from 11 to 44% in various series 2-4. Types of supraventricular arrhythmias seen in the setting of acute myocardial infarction are, atrial premature complexes, atrial fibrillation AF atrial flutter, paroxymal atrial tachycardia, junctional tachycardia and nodel rhythms.

Ambulatory electrocardiographic monitoring is an important diagnostic tool in patients with supraventricular arrhythmias the ambulatory, ECG can also be used to assess therapeutic procedures most sustained supraventricular arrhythmias are diagnosed upon presentation of the patients at a medical facility by recording (12 lead ECG, either alone or with an appropritate rythem strip.

However, transient arrhythmias may cause symptoms that may not last long enough for patients to travel to a medical facility to obtain on ECG for those patients the ambulatory ECG is critical for diagnosis if the arrhythmic events are sufficiently frequent in a 24 hour period, or if the expectation is that the arrhythmia will occur in 24 hour period than the contineus 24 hour ambulatory ECG is most useful.

The major current applications of ambulatory ECG monitoring of supraventricular arrhythmias includes -

1. Assessment of symptoms (Frequent, preferably daily) possibly associated with a transient arrhythmia.
2. Characterisation of known all suspected supraventricular arrhythmias.
3. Assessment of sinusnode dysfunction.
4. Correlation of effects of the activities of daily living with supraventricular arrhythmias.
5. Assessment of AV conduction.
6. Determination of the effectiveness of antiarrhythmic therapy.

In this study the Holter monitoring of patients of myocardial infarction and angina pectoris, the incidence of supraventricular arrhythmias in these groups (table VII). The presents study found that out of 19 patients MI only 1 patient had supraventricular premature beats (SVPBs) of grade II i.e. SVPBs >100) 17 patients of MI had no SVPBs in the range 0-5.

On the other hand out of 26 patients of angina pectoris only 4 patients had SVPBs of grade I (i.e. 5-100) and 23 patients had no SVPBs.

In this study it is apparent that there was no significant difference between incidence of supraventricular arrhythmias between patients of myocardial infarction and angina pectoris the reason for this could be is that as we have small number of patients under the study groups and as such the incidence of supraventricular arrhythmias are not high after myocardial infarction, which led almost equal incidence of SVPBs between the two groups.

Summary & Conclusion

SUMMARY AND CONCLUSION

The present study was carried out in the Department of Medicine M.L.B. Medical College, Jhansi the case material consisted of 45 consecutive patients, with coronary artery disease (angina/MI).

Out of 45 subjects 31 (68.88%) males and 14 (13.11%) females. Maximum number 13 (28.88%) were from 56 to 65 years of age. Mean age of patients in this group was 55.64±12.35 SD. years.

Majority of patients belonged to middle class and most of them were from urban.

In the present study risk factors fore CAD were present in good number of cases 91%. Cigarette smoking was observed to be the commonest risk factors 60%.

According to Kleiger et al present study distribution of HRV in 50-100 ms groups was 60% and in more than 100 ms was 40%. Distribution of subject according to their disease out of 45 cases 19 (42.22%) belongs to MI and 26 (57.77%) of angina pectoris. According to data post MI patients were found to have higher risk for mortality in comparison to angina. (Low the HRV higher the risk).

ST depression $\geq$ 1 mm was seen 42% patients of MI in comparison only 31.61% of patient of angina pectoris. The incidence of ambulatory significant ST depression was more in patients of MI then angina.

In this study 19 patients of MI 26 patients of angina on 24 hours Holter recording higher incidence of ectopics were seen 42% and 38.46% ventricular

couplets 42.10% and 27.92% and ventricular runs 21.05% and 23.07% respectively in patients of AMI and angina.

In this study there were no significant incidence of SVPBs in MI and angina patients.

This study conclude that all type of ventricular arrhythmias detected by AECG are more common in patients of MI in comparison to patient of angina pectoris so patient of MI are also indicate increased risk of mortality as compare to angina pectoris.

Thus in patients with CAD, there are three potential areas where an Ambulatory monitoring can be utilised diagnostic, prognostic and assessments of therapeutic efficacy. AECG for the diagnoses of CAD is not recommended routinely because of poor sensitivity and specificity except in those with chest pain suggestive of Prinzmetal's angina or those who are unable to exercise.

Analysis of rhythm and ST segment changes during AECG can provide additional prognostic information in various subgroups of CAD. However, other prognostic indicators like age, previous MI, left ventricular dysfunction and exercise induced ischemia are usually easier to obtain and more predictive of prognosis.

Heart rate variability analysis has come up as an excellent prognostic tool. Depressed HRV is a new and powerful risk factor for CAD. Predictive value of HRV is independent of other parameters established for post infarction risk stratification, such as left ventricular ejection fraction ventricular ectopic activity and late potentials for predictions of all cause mortality. Assessment of HRV and thereby autonomic activity is of great clinical significance, particularly in

certain clinical settings such as cardiac arrhythmias, cardiac failure and diabetic autonomic neuropathy. HRV is markedly reduced in patients with CHF.

A routine application for this indications can be recommended ACC /AHA task Force recommended. AECG monitoring in CAD for following indication 3. (American College, of Cardiology/American Heart Association Task Force JAM Coll Card. 1989).

A. Class -I Chestpain suggestive of prinzmetal's angina.

Class II Patients with chest pain who are unable to exercise.

B. For detection of silent ischemia in post MI patients who are known to have VPCs.

C. For risk Prediction in known CAD, anterior myocardial infarction. Stable or unstable angina when combined with confirmatory stress testing.

Class III Not indicated -

1. Chest pain evaluation : Typical or atypical

2. Ischemia detection in asymptomatic persons.

3. For risk prediction as a sole test.

Bibliography

BIBLIOGRAPHY

1. Reddy, KS Cardiovascular disease in India. World Health state Q. 1993;46:101-107.
2. Healthy People 2000; National health promotion and diseases prevention objectives.Washingtion (D.C) U.S Department of Health and human services. 1991:392-413;DHHS publication No. (PHS) 91 - 50212
3. Gupta R, Gupta VP. Meta-analysis reveals a rising coronary heart disease prevalence in India: increase is more in urban population, in men and at younger age (submitted for publication)
4. Kaul U, DograB, Manchanda SC, myocardial infarction in young Indian patients: risk factors and angiographice profile.Am Heart J 1986; 71:112-115.
5. Balarajan R Ethnic differences in mortality from ischemic heart disease and cerebrovascular disease in England and wales. Br Med J 1991;302:560-564.
6. Klatsky AL, Tekawa I, Armstrong MA, Sidney S. Americans born in India and Pakistan are at high risk of coronary disease hospitalization Circulation 1993;87,suppl 2:17.
7. Enas EA, Yusuf S, Mehta JL. Prevalence of coronary artery disease in Indians. Am J Cardiol 1992;70:945-949.
8. Hughes K, Lun KC, Yeo PPB. Cardiovascular disease in Chinese Malays and Indians in Singapore:I. Differences in mortality. J Epidemiol Comm Health 1990;44:24-28.

9. Rajadurai J, Arokiasami J, Pasamanickam K, Shatar A, Mei -Lin O. Coronary artery disease in s. Aust NZ J Med 1992;22:345-348.

10. Chadha S, Radhakrishnan S, Ramachandran K, Kaul U, Gopinath N. Epidemiological study of coronary heart disease in urban population of Delhi. Indian J Med D Res 1990;92:424-430.

11. Littler WA, Lawrence RE. Acute myocardial infarction is South Asians and Caucasians in Birmingham. Br Me J 1985;290:1472.

12. Jalowiec DA, Hill JA. Myocardial infarction in the young and in women. Cardiovasc Chin 1989;20197-206.

13. Wang XL, Tam C, Mc Credie RM, Wilken DEL. Determinants of severity of coronary artery disease in Australian men and women. Circulation 1994;89:1974-1981.

14. Mc Keigue PM, Ferrie JE, Pierpoint T, Marmot MG. Association of early-onset coronary heart disease in shouth men with glucose intolerance and hyperinusulinemia. Circulation 1993;87:152-161.

15. Pahlajani DB, Chawla MH, Kapashi KA. Coronary artery disease pattern in the young.J Assoc Phys Ind 1989;37:312-314.

16. Hughes LO, Raval U, Raftery EB: First myocardial infarction in patients with coronary artery disease. Int J Cardiol 1989;298:1345-1350

17. Lowry PJ, Lamb P, Mace PJE, Little WA, Pentecost BL, Influence of racial orgin on admission of patients with suspected myocadial infarction in Birminigham. Br. Heart J 1991; 66:29-35.

18. Negus BH, willard JE, Glamann DB, Landau C, Snider RW, Hillis LD, Lange RA. Coronary anatomy and prognosis of young, asymptomtic survivors of myocardial infarction. Am J Med 1994; 96:354-358.

19. Dave TH, Wasir HS, Prabhakaran D, Dev V, Das G, Rajani M, Venugopal P, Tandon R. Profile coronary artery disease in Indian women: correlation of clinical, noninvasive and coronary angiographic findings. Ind Heart J 1991; 43:25-29.

20. Sewdarsen M, Vythilingum S, Jialal I, Desai RK, Becker P,. Abnormalities in sex hormones are a risk factor for premature manifestation coronay artery disease in South Africa Indian men Atherosclerosis 1990; 83:1110117.

21. Pinto RJ, Bhagwat RJ, Loya YS, Sharma S. Coronary artery disease in premenopausal women : risk factors and angiographic profile. Ind Heart 1992; 44:99-101.

22. WHO (1982). Techn Rep. Ser No. 678 .

23. Sarvothan, S.G. and Berry, J.N. 1968 circulation, 37:339.

24. Dewan, B.D. et al (1974). Indian Heart J. 26:68.

25. Buja, L.M, and Mc Allister, H.A. Jr. Coronary artery disease: Anatomic abnormalities, In willerson, J.J, and Cohn, J.N.(eds): cardiovascular Medicine New York, Churchill Livingstone, 1995, p 316.

26. Harrison, D.C.: Nonatheeroscleroitc coronary disease, In Fuster, V.,Ross R., and Topol, E.J. (eds): Atherosclerosis and Coronary Artery Disease, Philadelphia, Lippincott- Raven, 1996,pp,757-772.

27. Conti, C.R.: Myocardial infarction: Thoughts about pathogenesis and the role of coronary artery spasm. Am Heart J 110:187,1985.

28. Vincent, G.M., Anderson, J.L. and Marshall, H.W.: Coronary spasm producing coronary thrombosis and myocardial infarction. N.eng. J.Med. 309: 320,1983.

29. Dollar, A.L. Pierre-Lonis, M.L. Mc Intosh, C.L., et al: Extensive multifocal myocardial infarcts from cloth emboli after replacement if mitral and aortic values with cloth covered caged ball prosthesis. Am.J. Cordiol.64.410,1989.

30. Ackermann, D.M.,Hyma,B.A. and Ed... W.D.: Malignant neoplastic emboli to the coronary arteries. Hum. Pathol 18:955,1987.

31. Obarski, T.P. Loop, F.D., Casgrone, D.M., et al: Frequency of acute myocardial infarction in valve repairs versus valve replacement for pure mitral regurgitation. A.M.J. Cardiol.65:887,1990.

32. Spodick, D.H.: inflamations and the onset of myocardial infarction. Ann. Intern Med. 99: 547,195.

33. Connolley, J.E. Eldridge, F.L., Calvin, J.W., et al.: Proximal coronary artery obstruction N. Engl. J. Med.271 : 213,1964

34. Roberts, W.C., Mac Gregor, R.R. DeBlane H.T.,et al : the prepulseless phase of pusleless disease, with pulses Am. J Med. 46:313, 1969.

35. Pick,R.A. Glover, M.U. and Vieweg, women with located coronary arteries. Chest 82 : 378,1982.

36. Van Camp, G, Deschamps, P., Mestrz, R.et al.:Adult onset Kawasaki disease diagnosed by the echocardiographic demonstration of coronary aneurysms. Eur. Heart J. 16: 1155,1995.

37. Lie, J.L., Failoni, D.D. and Davis, D.C.J.: Temporal arteritis with giant cell aortitis, coronary arteritis and myocardial infarction arch. Pathol. Lab. Med. 110: 857, 1986.

38. Joensuu. H.: Acute myocardial infarction after heart irradiation in young patients with Hodgkin's disease. Chest 95 : 388,1989.

39. Huang S., Kumar G., Steele, H.D. et al : Cardiac involvement in pseudoxanthoma elasticum. Am. Heart J. 74: 680,1967.

40. Inser, J.M., and Chokshi, S.K.: Cardiac Complications of Cocain abuse. Annur Rev. Med. 42: 133,1991.

41. Kloner, R.A., Hale, S. Alkev, K.,et al; The effects of acute and chronic cocaine use on the heart. Circulation 85 : 407, 1992.

42. Yeager, S.B. and Freed, M.D.: Myocardial infarction as a manifestation of polycythemia in cynotic heart disease Am. J. Cardiol 53 : 952, 1984.

43. Martin, C.R. Cabb. C. Tatter, D. et al: Acute myocardial infarction in sickle cell anemia, Arch. Intern. Med. 143:830-1983.

44. Bergeron, G.A. Goldsmith R., Schiller, N.B.: Myocaridal infarction severe, reversible ischemia, and shock following execess thyroid administration in a women with normal coronary arteries, Arch. Intern. Med. 145; 1450: 1988.

45. Carson, R., Oldroyd, K. and Phasdke, K. : Myocaridal infarction due to amphetamine BMJ 294:1525,1987.

46. Maller, J.E. Stone PH., Turi, Z.G. et al L Circadian variation in the frequency of onset of acute myocardial infarction N. Eng. J Med 313:1315, 1985.

47. Willich, S.N. Linderer, T., Wegscheider, K. et al Increasing morning incidence of myocardial infarction in the ISAM study : Absence with prior B-adrenergic blockade. Circulation 80 : 853, 1989.

48. Ridker, P.M. Manson, J.E., et al: Circadian variation of myocardial infarction and the effect of low dose aspirin in a randomized trial of physicians circulation 80:853, 1989.

49. Fallonn J.T.: pathology of myocardial infarction and reperfusion. In fuster, V., Ross, R., and Topol, E.J. (eds.) : Atheroscloresosis and Coronary Artery disease. Philadelphia, Lipincott-Raven, 1996, PP 791-796.

50. Yono, K., and Maclean, C.J.: The incidence and prognosis of unrecognized myocardial infarction in Honolulu, Hawii., Heart Program Arch. Intern. Med. 149: 1528, 1989.

51. Sigurdsson, B. Thorgeirisson, G., Sigweldason, H. et al.: Unrecognized myocardial infarction : Epidemiology, Clinical characterstics, and the prognositic role of angina pectoris : The Reykjavik study. Ann. Intern. Med. 122:96, 1995.

52. Cammarano G., Ragosta, M., Gimble, L.W., et al: Identification of viable myocardium with contrast echocardigraphy in patients with poor left vantricular systolic function caused by recent or remote myocardial infarction. Am. J. Cardiol. 75:215, 1995.

53. Finkelhor, R.S. Sun, J.P. Castellanos, M., et al.: Predicting left heart failure after a myocardial infarction: A preliminary study of the value of echocardiographic measures of left ventricular filling and wall motion. J. Am. Soc. Echocardior. 4:215, 1991.

54. Puleo, P.R. Guadago, P.A. Robert, R., et al.: Early diagnosis of acute myocardial infarction based on assay of subform of creatine kinase MB. Circulation 82: 759, 1990.

55. Marshall T, William J, and William K.M., Electrophoresis of serum enzyme and proteins followings acute MI J chromatogr, 1991; 569-323.

56. Adams, J., III Abendschein, D., and Jaffe, A.: Biochemical markers of myocardial injury : Is MB creatine kinase the choice for the 1990s? Circulation 88:750,1993.

57. Mair, J., Dienstl, F., Paschendorf, B.: Cardiac troponin T In the Diagnosis of myocardial injury. Crit Rev. Clin. Lab. Sci. 29:31, 1992.

58. Abe, S., Arnima, S., Yamashita, T., et al.: Early assessment of reperfusion therapy using cardiac troponin T.J. Am. Call. Cardiol 23:1382, 1994.

59. Apple, F.S. : Glycogen phosphorylase BB and other Cardiac proteins: Challenges to creatine kinase MB as the marker for detecting myocardial injury. Clin. Chem. 41:963, 1995.

60. de Vreede, J.J.M., Gorgels, A.P.M., Verstraaten, G.M.P., et: Did prognosis after acute myocardial infarction change during the past 30 years? A meta analysis J. Am. coll cardial. 18:698, 1991.

61. Gheorghiade, M: Razunma, P., Borzak S. et al: Deciline in the rate of hospital mortality from acute myocardial infarction; Impact of changing management strategies. Am Heart J. 131, 250, 1996.

62. Pell. S., and Fayerweather. W.E. Trends inthe incidence of myocardial infarction and in associte mortality and morbidity in a large employed population, 1957-1983 N. Eng. J. Med 312: 1005, 1985.

63. Younis, L.T., Miller, D.D., Chaitman, B.R.: preparative strategies to assess cardiac risk before noncardiac surgery. Clin cordiol. 18: 447 1995.

64. Mason, J.J., Owens, D.K. Harrims, R.A. et al: The role of coronary angiography and coronary revascularization before noncardiac vascular surgery. JAMA 273:1919, 1995.

65. Antman, E.M.: General hospital management. In Julian, D.G., and Braunwald, E. (eds) : Management of Acute Myocardial Infarction. Philadelphila, W.W. Saunders Company, 1994, p.29.

66. Rentrop, K.P.; Restoration of anterograde flow in acute myocardial infarction: The first 15 years. J. Am. Coll. Cardiol 25 : IS, 1995.

67. Yusuf, S., Wittes, J. Friedman, L: Overview of results of randomized clinical trials in heart disease. I. Treatment following myocardial infarction. JAMA 260, 2088, 1988.

68. Manoria PC, Pandey PK. Manoria P. CAD: Investigative Armamentarium at the turnof the millenium (Mellenium update cardiology) 74-76.

69. Hales S. Statical assays, Vol II, Haemastaticks, Innings and manby, Londan 1733.

70. Hon EH, Lee ST: Electronic evaluation of the fetal heart rate pattern Prededing fetal death, further observation AM. J. obstel Gyncol 87; 814-826, 1965.

71. Akselrod S, Gordon D, Ubel FA, Shannon DC, Barger AC. Power spectrum analysis of heart rate fluctuation : a quantitative probe of beat to beat cardiovascular control science 1981 213 (4504): 220-222.

72. Shannon DC, Carley DW Am J Physiol (Heart Cir Physiol) 1987, 22, 11874-11877.

73. Pomeranz B, Macaulay Am Physiol Heart Circ Phiol 1985-17H 151H 153.

74. Malpas SC purdi GL cardiovascular Res. 1990; 24: 210-213.

75. Lokhandwala YY, Rodrignez CM, Heart RAte Variability Indian Heart J 1994; 46:125.

76. Tamaki N, Yasuda T, Moore RH, et al. continuous measurement of left ventricular function by an ambulatory monitor in patients with coronary artery disease, J Nucl Med 1986; 27: 911 (Abst).

77. Levy D, Shapiro CM, Wright C, et al. The hemodynamic significance of asymptomatic ST segment depression assessed by ambulatory pulmonary artery pressure monitoring. Br Heart J 1986; 56:526-530.

78. Mulcahy D, Keegan J, Sparrow J. et al. Ischemia in the ambulatory setting - the total ischemic burden : Relation to exercise testing and

investigative and therapeutic implications J Am Coll Cardiol 1989; 14: 1166-72.

79. Mulcahy D, Parameshwer J, Holdright D, Value of ambulatory ST-segment monitoring in patients with chronic stabe angina: Does measurement of "total ischemic burden" assist with management ? Br Heart J 1992; 67:47-52.

80. Paul SD, Orav EJ, Glessan RE, Nesto RW. Use of exercise test parameters to predict presence and duration of ambulatory ischemia in patients with coronary artery disease. Am J Cardil 1994; 47 (10) 991-6.

81. Kalrissen JE, Bjorkhoim A, Blomstrand P. et al. Ambulatory ST recording has no additional value to exercise test for identification of severe coronary lession after an unstable coronary disease in men. Int. J Card imaging 1993; 9:281-9.

82. Rocco MB, Nabel EG, Campbel S, et al. Prognostic importance of myocardial ischemia detected by ambulatory monitoring in patients with stable coronary artery disease. Circulation 1988; 78:877-884.

83. Deedwania PC, Carbajel EV. Usefulness of ambulatory silent myocardial ischemia added to the prognostic value of exercise test parameters in predicting risk of cardiac death in patients with stable angina pectoris and exercise induced myocardial ischemia. Am J Cardil 1991; 68:1279-86.

84. Tzivoni D, Weisz G, Gavish A, et al. Comparison of mortality and myocardial infarction rates in stable angina pectoris with and without ischemic episodes during daily activities. Am J cardil 1989; 63 273-276.

85. Deedwania PC, Carbajal EV. Silent ischemia during daily life is independent predictor of mortality in stable angina. Circulation 1990; 81: 748-756.

86. Tzivoni D, Ganesh A, Zin D. et al. Prognostic significance of isshemic episodes in patients with previous myocardial infarction. Am J Cardil 1988; 62:661-664.

87. Langer A, Minkowith T. Doni P. et al. Tissue plasminogen activator: Toronto (TPAT study group. Pathophysiology and prognostic significance of Holter detection of ST- segment depression after myocardial infartion. AM J. Caril 1994; 73:747-752.

88. Goodman SG. Freeman MR, Armstrong PW, Langer A. Does ambulatory nonitoring contribute to excerise testing and myocardial perfusion scintigraphy in the prediction of the extent of coronary artery disease in stable angina Am J Cardil 1994; 73:747-752.

89. Deedwania PC. Comparison of the prognostic value of ischemia during daily life and ischemia induced by treadmill testing. Am J Cardil 1994; 73:15B-18B.

90. Heblad B, Junt Moller S. Svenssor K, et al. Increased mortality in men with ST-segment depression during 24 hours ambulatory long term ECG recording Results from prospective population study 'Men born in 1914' from Mlmo, Weden. Eur Heart J 1989; 10: 149-158.

91. Mangano DT, Browner WS, Hollenberg M, et al. Association of perioperative myocardial ischemia with cardiac morbidity and mortality in men undergoing non-cardiac surgery. N Eng J Med 1990; 323:178-88.

92. Algra A, Tissen JG, Roelandt JR, et al contribution of 24 hour electrocardiogram to the detection of sudden coronary death. Br. Heart J 1993; 70:42, 1-7.

93. Pepine CJ, Cohn PF, Deedwania PC, et al for the ASSIST study group effects of treatment on outcome in asymptomatic and mildly symptomatic patinets with ishemia druing daily life. The atenolol silent ischemia study (ASIST). Circulation 1994; 90:362-8.

94. Knatierud Gl, Bourassa MG, et al for the ACIP investigators. Effects of treatment strategies to suppress ischemia in coronary artery disease patients. 12 weeks results of the asymptomatic cardiac ishemia pilot (ACIP) J Am Coll Cardiol 1994; 24:11-20.

95. Marmur JD, Freeman MR, Langer A, et al prognosis in mediaclly stabilized unstable angina Early Holter ST- segment monitoring compared with abmulatory myocardial ischemia in the general population presenting with angina pectoris. J Am Coll Cardil, 1994; 23:74-81.

96. Gandhi MM, Wood DA, Lampe FC. Characteristics and clinical significance of ambulatory myocardial ischemia in the general population presenting with angina pectoris. J Am Coll Cardiol 1994; 23:74-81.

97. Gottieb SO, Weisfeldt M, Quyang P, et al. Silent ischemia as marker for early ufavourable outcomes in patients with unstable angina. N Engl med 1986; 314: 1214-1219.

98. Gotttieb SO, Weisfeldt Mr, Ouyang P, et al. Silent ischemia predicts infarction and death during 2 year follow-up of unstable angina. J Am Coll Cardiol 1987; &: 10, 756-60.

99. Nademanee K, Intrachot V, Joesphson MA, et al. Prognositic significance of silent myocardial ischemia in patients with unstable angina. J Am Coll Cardil 1987, 10: 1-9.

100. Langer A. Singh N. Freeman MR, Detection of silent ischemia adds to prognostic value of coronary anatomy and left ventricular function in predicting outcome in unstable angima patients. Can J Cardil 1995; 11:117-122.

101. Goldgerg AD, Jafri S. Polance G. et al. ST depression on Holter monitoring during hospitalization for acute myocardial infarction does not predict subsequent cardiac events J Am Coll Cardiol 199; 17:66A (Abstr).

102. Arstall MA, Barromer FA, Horonitz JD. Silent ischemia after uncomplicated myocardial infarction : lack of clinical significance. Int. J Cardil 1994; 45:45.

103. Gottieb SO, Tottieb SH. Achuff SC, et al. Silent ischemia on holter monitoring predicts mortality in high risk post infarction patients. JAMA 1989; 295:1030-1035.

104. Tzivoni D. Gavish A. Zin D. et al Prognostic significance of ischemia episodes in patients with previous myocardial infarction. Am J Cardil 1988; 62:661-664.

105. Dorian P. Lenger A, Morgan C, et al Importance of ST segment depression as a determinant of ventricular premature complex frequency after thrombolysis for acute myocardial infarction Tissue Plasminogen Activator. Toranto (TPAT) study group. AM J Cardil 1994; 74;419-23.

106. Stevenson RN, Merchant BG, Rajadjalank et al. Holter ST monitoring early after acute myocardial infarction. Mechanism of ischemia in patients treated by thrombolysis. Br. Heart J 1993; 70:433-7.

107. Krucoff MW, Green CE, Satlav LF, et al. Non-invsive detection of coronary artery patency using continuous ST- segment monitoring Am J Cardil 1986; 57: 916 - 922.

108. Kennedy HL, Sciler SM, Sprague MK, et al. Relation of silent myocardial ischemia after coronary artery bypass grafting to angiographic completenss of revascularisation and long term prognosis Am J Cardiol 1990; 65:14-22

109. Hoberg E, Schwarz F, Vogenreiter U, et al. Holter monitoring before, during and after percutaneous transluminal coronary angioplasty for evaluation of high resolution trend rcording of leads CM5 and C5 for ST-segment analysis AM J Cardiol 1987; 60 : 796.

110. Patel D, Mulcahy D, Cenazen N, et al. Prognostic significance of transient ST segment changes after coronary artery bypass surgery: A longterm (4-10 years) follow up study. Br. Heart J 1993; 70:41.

111. Ruberman W. Weinblott E, Goldberg JD, et al. Ventricular prfemature beats and mortality after acute myocardial infarction. N Eng J Med 1977; 297:750-7.

112. Moss AJ, Davis HT, Decemilla J, Bayer LW. Ventricular ectopic beats and their relation to sudden and non-sudden cardiac death aftger myocardial infarction. Circulation, 1979, 60:998, 1003.

113. Mukharji, J, Rude RE, Pool WK, et al and the MILIS study group. Risk factors for sudden death after myocardial infarction: two year follow up. AM J Cardil 1984 :54:37-6.

114. Koster JB, Buingtor R, Fridman LM, et al. Prognostic significance of ventricular ectopic activity in survivors of acute myocardial infarction. J Am Coll cardiol 1987; 10:231-42.

115. Bigger JT Jr, Fleise JL. Kloner K, et al. The Multicentre Post-infarction Research Group. The relationship between ventricular arrythmias, left ventricular dysfunction and mortality in the two years after myocardial infarction. Circulation: 1984; 69:250-258.

116. Maggioni AP, Jaunetti G. Franzosi MG, et al. Prevelence and prognostic significance of ventricular arrythmias after acute myocardial infarction in thrombolytic era. Circulation. 1993; 87:312-332.

117. Kennedy HL. Chendra V, Sayiner KL, et al. Effectiveness of increasing hours of continous ambulatory electrocardiography in detection of maximal ventricular ectopy. Am J Cardiol 1978; 42:925-30.

118. Petritta M, Bianchi V, Pulcino A. Continuous electrocardiographic monitoring for more than one hour does not improve the prognostic

value of ventricular arrythmias in survivors of first acute myocardial infarction Am J Cardiol 1994:73:139-42.

119. Moser M, Lehofer M, Sedurinek a, et al. heart rate variability as a prognostic tool in cardiology. A contribution to the problem from a theoretical point of view. Circulation 1994; 90:1078-82.

120. Bigger Jt. Fleiss JL, Steiman RC. et al PR variability in healthy, middle-aged persons compared with patients with chronic coronary heart disease or recent acute myocardial infarction. Circulation 1995; 97:1936-1943.

121. Huikiri HV, Niemela MJ, Ojala S. Circadian rhythms of frequency domain measures of heart rate variavility in healthy subjects and patients with coronary artery disease. Effects of arousal and upright posture. Circulation 1994; 90:1210126.

122. Carolo GC, Stroder P, Sulla A. heart Rate Variability before the occurence of silent myocardial inshemia during ambulatory monitoring. Am J Cardiol 1994; 73 : 845-9.

123. Goseki Y, Masubara T, Takahashi N, et al. Heart rate variability before the occurence of silent myocardial ischemia during ambulatory monitoring. Am J Cardiol 1994; 73:845-9.

124. Tsuji HT, Venditti FJ, Menders ES, Evans JC, et al. Reduced heart rate variability and mortality risk in an elderly cohort. The Framingham Heart Study. Circulation 1994; 90:878-883.

125. Patretta M, Marciano F, Mgaux Ml, et al. Efects of coronary angioplasty on heart rate variability explored in the domain of time and frequency in patients with one vessel coronary disease. G0ltal-Cardiol 1994; 24:973.

126. Lorcchino Ml, Diclemente D, Saccone V, et al. An analysis of the variability of the heart rate and its significance in the risk stratification of patients with unstable angina. Cardiologia 1994; 39:35-43.

127. Vallkama JO, Huikuri HV, Airksinen KE, et al. Determinats of frequency domain measures of heart rate variability in the acute and convalescent phases of myocardial infarction. Cardiovasc Res. 1994;28:1273.

128. Valkamma JO, Huikuri HV. Koistinem MJ, et al. Relation between heart rate variability and spontaneous and induced ventricular arrythmias in patients with coronary artery disease. J Am Coll Cardiol. 1995; 25(2):437-443.

129. Odemujiwa O, Pobniecki J, Malik M, et al. Temporal influences on the prediction of postinfarction mortality by heart rate variability. A comparison with the left ventricular ejection fraction Br. Heart J 1994; 71: 521-7.

130. Vaishnave S, Stevenson R, Marchent B, et al. Relation between heart rate variability early after acute myocardial infarction and long term mortality. Am J Cardiol. 1994; 73: 653-657.

131. Pediretti RF, Colombo E, Sarzi Braga S, et al. Efect of thrombolysis on heart rate variability thrombolytic life threatening ventricular arrythmia in surviviors of acute myocardial infarction. J Am Coll Cardiol 1994; 23:19-26.

132. Zabel M, Kliengenheben T, Hohnlosev SH. Changes in autonomic tone follwing throbolytic therapy for acute myocardial infarction; Assessment by analysis of heart rate variability. J Cardiovasc. Electrophysiol. 1994; 5:21-28.

133. Merchant B, Stevenson R, Vaishnave S, et al. Myocardial inshemia and angina in the early post infarction period: A comparison with patients with stable coronary artery disease. Br. Heart J 1993; 70:438-422.

134. Niemela Mj, Arksiver KE, Huikuri HV. Effect of beta blockeade on heart rate variability in patients with coronary artery disease. J. Am. Coll Cardiol 1994; 23:1370-1377.

135. Sandrone G, Mortars A, Torzillo D, et al. Efects of beta blockers (atenolol or metoprolol) on heart rate variability after acute myocardial infarction. Am. Coll Cardiol 1994; 74:340.

136. Berisso M Carratino L, Ferroni A, Frequency, charecteristics significance of S.V.T. detected by 24 hours electrocardiographic recording in the late hospital phases of acute MI. Am J cardiol 199; 65:1065.

137. Akselrod S. Gardon D. Ubel FA. Shannon DC, Barger AC, Power spectrum analysis of heart rate fluctuation aquantitative prove of beat-to beat cardiovascular control. science 1981; 213:220-222.

138. Malliani A. Pagnani M. Lombardi F, Cardiovascular neural regulation explored in the frequency domain. Circulation 1991; 84:482-492.

139. Van Ravenswaaij-Arts CMA, Kolleee LAA, Heart rate variability. Ann Intern Med 1993:118:436-447.

140. Pomeranz B. Macaulary RJ, Caudill MA, Assessment of autonomic function in human by heart rate spectral analysis. Am J Physiol 1985; 248:H151-H153.

141. Kleiger RE, Miller JP. Bigger JT. Moss AJ, The multicentre post infarction research group decrease heart rate veriability and its association with increased mortality after acute MI. Am J cardiol 1987; 59:256-262.

142. Bigger JT, Fleiss JL, Steinman RC, Frequency - domain major of heart period variability and mortality after MI. Circulation 1992; 85:164-171.

143. Farrel TG, Bashier, Y, cripps T. Risk stratification for arrhythmic event in postinfarction patients based on heart rate variability AECG variables and the signal averaged electrocardiogra. J Am Koll Cordiol 1991; 18:687-697.

144. Singh N. Mironow D, Armstrong PW. For the GUSTO ECG Substudy Investigators HRV assessment early after AMI. Pathophysiological and prognostic correlates. Circulation 1996; 93:1388-1395.

145. Kleiger RE, Stein PK, Bosner MS. Time domain measurements of heart rate variability. Cardiol Clin 1992; 10:487-99.

146. Kleger RE, Miller JP, Bigger JT, Decreased HRV and its association with increased mortality after AMI. Am J Cardiol 1987; 59:256-62.

147. Cripps TR, Malik M, Farrell TS, Prognostic value reduced heart rate HRV after MI clinical evaluation of a new analysis method. Br Heart J 1991; 65:14-9.

148. Bigger JT, Fleiss J, Steinman RC, Rolnitzyky LM, Kleiger RE, Rottman JN, Frequency domain measures of heart period variability and mortality after MI. Circulation 1992; 85:164-71.

149. Farrel TG, Bashir Y, Cripps T, Malik M. Risk stratification for arrhythmic events in post infarction patients based on HRV ambulatory electrocardiographic variables and the signal - averaged electrocardiogram. J Am coll Cardil 1991; 18:687-97.

150. Rich MW, Saini JS, Kleiger RE. Correlation of HRV with clinical and angiographic variables and late mortality after coronary angiography. Am J cardill 1988; 62:59-66

151. Vinder T, Frey B. Porenta G. Heinz G, Prognostic value of HRV in patients awaiting cardiac transplantationPACE 1992;15:2215-20.

152. Odemuyiwa O, Malik M, Farrel T, comparison of the predictive characteristics of HRV index N. left ventricular ejection fraction for all cause mortality arrhythmic event and sudden death after acute MI. Aj cardiol 1991; 68:434:439.

CARDIOLOGY DIV, DEPT. OF MEDICINE

M.L.B. MEDICAL COLLEGE, JHANSI,U.P.,INDIA

Phone: 0517-441610 Fax: 0517-440858

HOLTER ECG SUMMARY REPORT

Patient Name: Prasad, Madhav
Address: Village Buana,Jhansi
Supervising Physician: Dr.PRAVEEN KUMAR JAIN ,MD,DM.
Referred By: Dr. P. Kumar DM
Start Time: 16:00
Indications: Ac. Ant. Wall M.I
Medications: T.Monit,T.Ecosprin,T.Metolar,T.Isordil

ID:
Age: 45 Weight:
Sex: M Height:
Recording Date: 25/10/2000

HEART RATE	
Average HR:	63
Min HR: (4 Beat)	48 at 16:32
Max HR: (4 Beat)	128 at 20:45
Min Hourly HR:	56 at 16:00
Max Hourly HR:	78 at 20:00
Total Beats:	56462
Minutes Analyzed:	916

VENTRICULAR ECTOPIC	
VE Total:	19
VE Pair Total:	0
V-Run Total:	0
VE's per 1,000:	0
Min HR V-Run	N/A
Max HR V-Run	N/A
Longest V-Run	N/A

SUPRA VENTRICULAR ECTOPIC	
SVE Total:	3
SV-Run Total:	0
SVE's per 1,000:	0
Max HR SV-Run	N/A
Longest SV-Run	N/A
Aberrant Beats:	0

ST SEGMENT
Ch. 1 Total ST Minutes: 0
Ch. 2 Total ST Minutes: 0
Ch. 3 Total ST Minutes: 0
No ST Episodes
No ST Minutes

HEART RATE VARIABILITY	
SDNN:	131
SDANN Index:	90
SDNN Index:	87
rMSSD:	51
pNN50:	29

CONDUCTION & QT	
Pauses > 2.5 Seconds:	0
Longest Pause:	N/A
Long QT Interval:	356 ms (Ch. 1)
Corrected QT Interval:	337 ms
Long QT Interval at 17:04. Heart Rate 54 bpm.	

CONCLUSIONS:

The average heart rate was 63, with a minimum of 48 and a maximum of 128. Ventricular ectopic beats totaled 19, with 0 VE Pairs and 0 V-Runs. SupraVentricular ectopics totaled 3, with 0 SV-Runs. Pauses in excess of 2.5 seconds totaled 0. The number of minutes of analyzed ECG data was 916.

ST episode minutes totaled 0.

SIGNATURE: